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BRAIN ABSCESS DUE TO THE FUNGUS HORMODENDRUM

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Brain abscess caused by fungal infection is rare, only very few examples having been recorded in the English language literature. Perhaps the most comprehensive review is that of Craig and Gates,[1] who investigated all cases of brain abscess occurring in the Mayo Clinic during the years 1915-1945. During this 30-year period there were 104 examples of metastatic brain abscess, only 5 of which were caused by fungal infection. Two of these were caused by *Actinomyces* species, two by *Coccidioides immitis* and one by *Monilia albicans*. Apart from this series only isolated cases have been reported, mainly due to *Actinomyces*, *Blastomyces* or *Torula* species. Eckhardt and Pilcher[2] described a case caused by *Nocardia asteroides*.

Binford *et al.*[3] reported the case history of a patient with a metastatic brain abscess caused by the fungus *Cladosporium* (*Hormodendrum*) *trichoides*. King and Collette[4] described a second example of brain abscess due to this fungus and the former authors demonstrated the identity of the fungus isolated by King and Collette with that which they had isolated.

The case history reported here is a further example of a brain abscess due to a fungus of the *Hormodendrum* group and is, as far as we are aware, only the third case described.

CASE REPORT

W.P., a Bantu male aged 30 years, was admitted to hospital in a state of mental confusion. This state alternated with lucid intervals of a few hours' duration during which he complained of headache and pains in the chest and in both knees. These symptoms had been present for about 10 days. The headache was occipital and was continuous. It was not possible to obtain any further history apart from these meagre details.

The patient was a well-built man. Normal temperature and pulse rate. There was a small superficial ulcerated area, shallow, and about 1 inch in diameter, on the left side of the scalp over the temporal region. There was marked neck stiffness and both Kernig's and Brudzinski's signs were positive. All the cranial nerves appeared to be intact. The deep reflexes were extremely brisk and both plantar responses were equivocal. Motor power, sensation and proprioception were intact in all limbs.

Examination of other systems was essentially negative. The blood pressure was 128/80 mm. Hg.

Lumbar puncture revealed a slightly hazy fluid under increased pressure. The protein content was 70 mg.%, chlorides 650 mg.% and sugar 60 mg.%. The white-cell count showed 520 polymorphonuclear cells per c.mm. and 200 lymphocytes per c.mm. A Gram-stained film did not reveal any organisms in the spun deposit and culture of the cerebrospinal fluid was sterile.

A provisional diagnosis of tuberculous meningitis was made on admission and treatment was instituted with streptomycin and isoniazid. However, there was no response to this regime. The patient remained in a confused state with occasional bouts of pyrexia to 100·0°F. A fairly rapid deterioration in his condition took place and death occurred 2 weeks after admission.

Autopsy Report

The body was that of a well-built African male. There was no evidence of any skin rash apart from the ulcerated region on the left side of the scalp. Thick pleural adhesions were present on both sides and the lungs showed hypostatic congestion. The liver was enlarged and pale. There was a single horseshoe kidney with a solitary ureter coming off the lower portion of the kidney on the right side.

On the skull being opened the meninges appeared to be normal. When the dura was removed from the right side there was found to be some flattening of the cerebral gyri of the frontal lobe, with obliteration of the sulci. Embedded deep in the right frontal lobe was an abscess cavity containing thick creamy-coloured pus. The cavity was about 2 inches in diameter and was lined with ragged, necrotic fragments of brain tissue. The remainder of the brain appeared to be normal.

Histology. Sections were prepared from the wall of the abscess cavity and stained in the usual way with haematoxylin and eosin. The wall of the cavity contained many multinucleated cells of Langhan's type along with plasma cells, polymorphonuclear cells, lymphocytes and eosinophils. Numerous dark-brown fungal spores were also present in the wall and in the exudate in the cavity. These spores were from 6-15μ in diameter and were thick walled. They tended to be arranged in clusters, in some cases of up to 20 or 30 spores. Others were arranged in short chain formation of 5-6 spores. Many of them showed an appearance of septation.

Mycology. Culture of the pus on Sabouraud's agar resulted in relatively slow-growing colonies. After 14 days these were about 4 cm. in diameter and were of a dark olive-grey colour. In the early stages of growth the surface of the colonies was velvety smooth with a well-marked fringe of mycelial growth. After 3 weeks' incubation the surface of the colonies showed some radial striation. Culture of the pus on the polysaccharide medium of Nickerson and Mankowski gave rise to similar types of colonies, except that growth was a little faster than on the Sabouraud's agar and the colony colour was of a lighter olive shade.

Slide culture preparations on Sabouraud's agar were examined daily. After 4 or 5 days these showed brown-coloured, smooth-walled septate hyphae about 1·5-2·0μ in width. Arising from the hyphae were septate conidiophores bearing spores in long chain formation. The appearances were typical of fungi of the hormodendrum type.

Animal inoculation. A saline suspension from the fungal growth on the Sabouraud's agar was injected subcutaneously into the shaved abdomen of a guinea-pig and also intravenously into a rabbit. After 7 days the animals were sacrificed and examined. No lesions were found in the guinea-pig's organs and the site of injection showed only a restricted oedematous area about 1 cm. in diameter. The rabbit, however, showed multiple small abscesses in the liver, in the cortex of both kidneys and in the spleen. These consisted of collections of polymorphonuclear cells, lymphocytes, plasma cells and multinucleated cells. The typical brown fungal spores were present in large numbers. No lesions were present in the brain.

DISCUSSION

Fungi of the genus *Hormodendrum* are the cause of chromoblastomycosis in man. The term *Cladosporium* is preferred by some, and Binford *et al.*[3] maintain that 'hormodendrum' is an invalid synonym for 'cladosporium'. Chromoblastomycosis is common in tropical and sub-tropical areas and particularly in this part of the world. The condition is characterized by a chronic granulomatous infection of the skin, usually secondary to some form of trauma. The lower limbs are most commonly affected. The lesions progress slowly with the formation of ulcerated papillomatous nodules. Early lesions may simulate dermatophytosis and the later lesions have to be distinguished from tuberculosis verrucosa cutis, late nodular syphilis, yaws, leishmaniasis and maduromycosis.

Apart from the two cases of brain abscess already mentioned as resulting from *Cladosporium trichoides*, metastatic infection with fungi of the chromoblastomycosis group appears to have been recorded on only 2 occasions. Montpellier and Catanei[5] described a patient with metastatic lesions in the quadriceps and Carrion[6] recorded the case history of a patient with primary lesion on one leg and a subcutaneous nodule in the opposite thigh and another in the left forearm.

The strain of *Hormodendrum* described by Binford *et al.*[3] differed in certain respects from the strains usually found in chromoblastomycosis of the skin in man. Thus the spore chains were of greater length, and showed less frequent branching. In addition, the conidia were smaller than in the other pathogenic species. They compared the cultural features of the fungus which they isolated with those of a number of saprophytic strains isolated from fruit and other sources, but without being able to establish its identity with any of these. Intravenous injection of their fungus into rabbits resulted in the production of multiple brain abscesses.

Clinically, the patient described here did not appear to have cutaneous chromoblastomycosis. The small ulcerated area on the scalp was unfortunately not examined for the presence of fungi but its appearance was unlike that of chromoblastomycosis, though it may have been an early lesion.

SUMMARY

An example of brain abscess caused by the fungus *Hormodendrum* is described. Fungi of this type are the cause of chromoblastomycosis in man.

We wish to thank Dr. J. L. Parker, Director of Medical and Health Services, Natal, for permission to publish this case history.

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L. M. Marchand
Associate Secretary

Medical House
35 Wale Street
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15 October 1957

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15 Oktober 1957

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EDITORIAL

REDUCING DIETS

It has long been known that restriction of calorie intake is the most important factor in the loss of excess weight. The traditional medical advice to patients wanting to reduce always includes a diet sheet which, if it is scrupulously followed, cuts down the calorie intake to below the level supposed to be necessary for the maintenance of a dietary equilibrium. Experience has shown that this measure does not always lead to weight loss. Although discrepancies are usually attributed to failure or inability of the patient to carry out his instructions, the frequency of the experience has been noted. Moreover, slight departures from—not restrictions of—the normal diet appear sometimes to lead to loss of weight, and one set of workers found in a test series that persons on a high-fat diet lost weight more rapidly than those on high-protein or high-carbohydrate diets.[1] This uncertainty led Kekwick and Pawan[2] to examine the relation of calorie intake to obesity a little more closely. The question that these workers set themselves to answer was this: Is it the restriction of total calorie intake that causes the weight loss, or is it the alteration in proportions of carbohydrate, fat and protein in the diet?

The normal sedentary worker, it is usually stated, takes his daily 2,200 calories as 12% of protein, 24% of fat and 64% of carbohydrate, while the average reducing diet (yielding about 1,000 calories a day) consists of protein, fat and carbohydrate in about equal percentages. Kekwick and Pawan's experiment was conducted on cases of obesity in a hospital ward under the most favourable conditions; none of the patients could 'sneak' any food and rigid biochemical controls (water retention, nitrogen balance, fat absorption) were performed. The patients fell into 3 groups for the purposes of the experiment, viz.:

1. A group fed on a diet of which the component proportions were the same (protein 20, fat 33, carbohydrates 47), but the total amounts varied (500, 1,000, 1,500 and 2,000 calories).

2. A group fed on a diet of which the total calorie content was fixed (1,000 calories) but the components varied. Three different diets were used, each of which consisted of 90% of one component.

3. A group whose diet was stabilized on a normal (2,000

VAN DIE REDAKSIE

VERSLANKINGSDIËTE

Dit is reeds lank bekend dat 'n beperking van die kalorie-inname die belangrikste faktor by die vermindering van oortollige gewig is. Die tradisionele mediese raad aan pasiënte wat wil verslank sluit altyd 'n gebalanseerde dieetskema in wat—mits dit nougeset gevolg word—die kalorie-inname kortsny tot minder as wat nodig is om 'n dieetbalans te handhaaf. Die ondervinding het egter geleer dat hierdie maatreël nie altyd daarin slaag om die gewig te verminder nie. Afwykings word gewoonlik daaraan toegeskryf dat die pasiënt nie sy instruksies kon of wou uitvoer nie, maar daar is reeds opgelet dat die verskynsel (dat die gewig nie op so 'n dieet verminder nie) heel dikwels voorkom. Dit blyk selfs dat klein veranderings in die normale dieet, en nie soseer inkortings nie, soms 'n vermindering van gewig in die hand werk, en een groep navorsers het in 'n reeks toetse uitgevind dat persone op 'n vetryke dieet vinniger verslank het as dié wat 'n proteïen- of koolhidraatryke dieet gehou het.[1] Dit was hierdie onsekerheid wat Kekwick en Pawan[2] aangespoor het om die verhouding tussen kalorie-inname en vetsug nader te ondersoek. Hierdie navorsers het hulle dit ten doel gestel om die volgende vraag te beantwoord: Is dit die beperking van die totale kalorie-inname wat verslanking veroorsaak, of is dit 'n verandering in die verhouding van koolhidraat, vet en proteïen in die dieet?

Die normale ‚sittende' werker se daaglikse 2,200 kalorieë bestaan na bewering uit 12 persent proteïen, 24 persent vet en 64 persent koolhidraat, terwyl die gemiddelde verslankingsdieet (omtrent 1,000 kalorieë daagliks) uit proteïen, vet en koolhidraat in omtrent ewe groot persentasies bestaan. Kekwick en Pawan se eksperiment op vetsugtige pasiënte is in 'n hospitaal, onder die gunstigste toestande gedoen; nie een van die pasiënte kon skelmpies kos in die hande kry nie, en streng biochemiese kontroles (waterterughouding, die stikstof-balans, en vetabsorpsie) is toegepas. Die pasiënte is in 3 groepe verdeel vir die doeleindes van die toets:

1. 'n Groep gevoed op 'n dieet waarvan die samestellende proporsies dieselfde was (proteïen 20, vet 33, koolhidraat 47) maar waar die totale hoeveelhede verskil het (500, 1,000, 1,500 en 2,000 kalorieë).

2. 'n Groep op 'n dieet waarvan die totale kalorie-inhoud vasgestel was (1,000 kalorieë) maar waar die samestellende voedseltipes verskil het. By hierdie groep is 3 verskillende diëte gebruik, elk bestaande uit 90 persent van één van die samestellende voedselsoorte.

3. 'n Groep met 'n dieet wat vasgestel was op 'n normale daaglikse dieet van 2,000 kalorieë. Hulle is later verander na 'n dieet van 2,600 kalorieë, afwisselend ryk aan vet en aan koolhidraat, om vas te stel of hulle verslank het—

calories) daily diet. They are changed to a 2,600-calorie diet, alternatively of high-fat and high-protein composition, to see whether they lost weight in confirmation, more or less, of the results in group 2.

Although the entire experiment was neither large nor prolonged, it appears to have been conducted with a thoroughness that makes the results noteworthy, even if they do not find general acceptance.

The results of the first series bore out the generally-accepted view that the less a person eats the faster he will lose weight. By making weekly alterations in the total daily calorie intake of each patient, Kekwick and Pawan demonstrated a clear proportional relationship between intake and weight loss. The second series yielded more interesting results. Here the total calorie intake could still be regarded as a reducing diet (1,000 calories), yet the patients on the 90% carbohydrate diet lost no weight at all whilst the losses of those on the 90% protein diet and 90% fat diet were marked. Some patients of the latter groups lost 1-1½ lb. a day. The response of patients in the third group provided confirmation of Kekwick and Pawan's thesis that—within limits—it is the substance of the diet that is important rather than the amount. By feeding with 600 calories over the 'normal' they recorded actual losses in weight in some of their patients, provided the whole diet was a high-fat or a high protein one.

By means of biochemical checks that they carried out in these experiments Kekwick and Pawan were able to show that there was no defective absorption to account for the weight loss, nor any significant loss of carbohydrate stores or body protein. Slightly less than half the weight lost was shown to be due to loss of body water, and 50-70% to loss of body fat. The rate of insensible water loss is greater with high-fat and high-protein diets; this fact, together with the marked variations in weight loss between the different constant-calorie diets, is taken to suggest that obese persons alter their metabolism in response to variations in the diet. Kekwick and Pawan draw no practical conclusions from their experiments, and they have been taken to task for its brevity, 7-9 days being very short periods for studying changes of weight in obesity,[3] and for their conclusions over the role of body water in weight loss. From their own data the striking increase in insensible water loss would itself account for about 70% of the weight lost with the high-protein or high-fat diets, and proportionally less therefore would be due to loss of body fat.

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3. Hervey, G. R. (1956): *Ibid.*, **2**, 355.

hierdie deel van die toets was gedoen om die resultate van die tweede groep min of meer te bevestig.

Die hele eksperiment was maar kort en het nie baie persone ingesluit nie, maar dit blyk nogtans dat die navorsers só deeglik was dat die uitslae van hulle toets tog die aandag verdien, al word hulle nie algemeen aangeneem nie.

Die resultate van die eerste serie bevestig die algemene opvatting dat hoe minder 'n mens eet, hoe vinniger word hy maerder. Met hulle weeklikse veranderings in die totale daaglikse kalorie-inname van elke pasiënt, het Kekwick en Pawan 'n duidelike proporsionele verhouding tussen inname en gewigsvermindering aangetoon. Maar die resultate van die tweede serie was nog interessanter. In die tweede toets kon die totale kalorie-inname nog steeds as 'n verslankingsdieet beskou word (1,000 kalorieë daagliks) maar die pasiënte wat die 90 persent koolhidraat-dieet gehou het, het glad nie maerder geword nie, terwyl daar duidelike verslanking was by die pasiënte op diëte van 90 persent koolhidraat en 90 persent vet. Sommige van die pasiënte in die laasgenoemde twee groepe het tussen 1 en 1½ lb. per dag ligter geword. Die reaksie van die pasiënte in die derde groep het Kekwick en Pawan se vermoede bevestig dat (binne perke, natuurlik) die samestelling van die dieet meer belangrik is as die totale hoeveelhede. Met 'n dieet wat 600 kalorieë meer dan die ‚normale' bevat het, het hulle 'n gewigafname by sommige van hul pasiënte behaal mits die hele dieet 'n vet- of proteïenryke was.

Kekwick en Pawan was in staat om aan te toon deur middel van die biochemiese kontroles dat daar geen gebrekkige absorpsie was wat moontlik die gewigafname kon veroorsaak het nie, en dat die liggaamsreserwes van koolhidraat en proteïen nie merkbaar verminder het nie. Effens minder as die helfte van die gewigafname was klaarblyklik te danke aan die verlies van liggaamsvog, en 50 tot 70 persent was te danke aan die vermindering van liggaamsvet. Die spoed van onvoelbare waterverlies was vinniger by die vet- en proteïenryke diëte; hierdie feit, tesame met die duidelike variasies in die gewigafname tussen die verskillende kalorie-konstante diëte, word beskou as 'n aanduiding daarvan dat vet mense hulle metabolisme verander in reaksie op wysigings van die dieet. Kekwick en Pawan maak geen praktiese afleidings uit hulle navorsing nie; hulle is reeds oor die kole gehaal oor die kort duur van die eksperiment—7 tot 9 dae is maar kort om die veranderings in die gewig by vetsugtige pasiënte te bestudeer[3]—en ook oor hulle gevolgtrekkings insake die rol van liggaamsvog by verslanking. Bereken op hulle eie gegewens, kan die merkwaardige vermeerdering van onvoelbare waterverlies self verantwoordelik wees vir omtrent 70 persent van die vermindering in gewig op die proteïen- en vetryke diëte, en gevolglik speel die verlies van liggaamsvet na verhouding 'n kleiner rol by verslanking.

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SURVIVAL AT SEA

The physiological problems that arise in survivors of shipwreck or the ditching of aircraft have been studied by a number of investigators.[1] Apart from drowning or injury, in many cases death at sea has been due to exposure, and especially to inability to maintain the temperature of the body. When the body is immersed in cold water, heat is lost much more rapidly than when in air at the same temperature. This is due not only to the fact that water con-

ducts heat more readily than air, but also to the high specific heat of water. In general it has been found that heat balance is not maintained in water below about 20°C (68°F); the body temperature steadily falls until death eventually ensues. In freezing water, survival for about an hour may be expected. Shivering cannot prevent the fall in body temperature. The same danger of injury or death of the tissues occurs when limbs are immersed in cold water.

The muscular effort of swimming produces enough heat to balance the heat lost in ice-cold water and may maintain the normal body temperature for a short time. Further research is needed on this point, since there is the possibility that in thin individuals, who lack the insulation of a layer of fat, swimming may increase heat loss as well as heat production. Even when the body is not immersed in water, exposure in a cold environment such as cold air, especially if there is a wind, or snow and spray, or wet clothes, may render it impossible to maintain heat balance.

In hot climates an important physiological problem is loss of water and electrolyte balance. As much as 5 litres of sweat a day may be lost by a man lying on a raft in the tropical sun, and death might occur within two or three days. There is, however, less hazard in hot climates than in cold ones.

The clearer understanding of the physiological aspects of naval life-saving has lead to improvements in the design of equipment in rafts and lifeboats. The essential requirements are to give protection from water and cold, and in the tropics to provide shade and air movement. Specially designed suits, tents and rafts have been thoroughly studied under various climatic conditions.

The supply of water is the outstanding problem. Survival for 2 weeks without water is unlikely even in favourable circumstances. It has been found that carbohydrate (100 g. daily) reduces the break-down of protein and the output of urine; thus barley-sugar sweets will save more than their own weight of water. Other measures that may be adopted include the prevention of sea-sickness, the collection of rain water, and the chemical de-salting of sea water. The drinking of sea water must be forbidden. If a ration of fresh water is mixed with sea water it will not enable an individual to survive as long as the fresh water ration alone. Fish do not yield much water and the fluid obtained from them is not of favourable composition. As a food, fish contains much protein and need to be avoided unless plenty of fresh water is available.

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RAUWILOID IN HYPERTENSION

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Although *Rauwolfia serpentina* has been widely used in India for many years, it is only since Vakil's paper in 1949[1] that this drug has aroused pharmacological interest and has come into general medical use in the treatment of hypertension. During the few years that have elapsed since the first report on this subject a large volume of literature has accumulated and a number of different preparations have become available for the treatment of hypertension.

These preparations can be divided into 3 groups as follows: (1) Whole-root preparations (Serpina, Preparation 1043, Raudixin), (2) pure alkaloids (reserpine, rescinnamine), and (3) 'Alkaloidal extracts (Roxinil, Rauwiloid).

1. *Whole-root preparations* consist of powdered dried root. 'Serpina' is a preparation which was originally used in India, and was reported on in the earlier American communications.[1-2] Preparation 1043 (Riker) and Raudixin (Squibb) next became available.[3] Raudixin is still in common use where administration of a whole-root preparation is desired.

2. *Pure alkaloids.* The hypotensive action of *Rauwolfia serpentina* is due to its alkaloids, of which so far about 15 have been isolated.[4] Only 2 alkaloids that have been used in the pure form are so far available to the profession, viz. reserpine (Serpasil, Ciba) and rescinnamine (Riker).

3. *'Alkaloidal' extracts.* There is some evidence that other alkaloids apart from reserpine and rescinnamine exert a hypotensive action, and 2 alkaloidal extracts have become available, namely Roxinil (Merck) and Rauwiloid (Riker). Roxinil contains a number of alkaloids of reserpine-like action and a serpentine-like material. Rauwiloid is an extract of the alseroxylon fraction of the alkaloids, consisting of reserpine and rescinnamine, which provide about 60% of the activity, and other, as yet unidentified active alkaloids.

PHARMACOLOGICAL ASPECTS

Most of the detailed work on the action of *Rauwolfia serpentina* has been done with the pure alkaloid reserpine. It is now well established that it has a sedative and tranquillizing action on the central nervous system, which is quite different from the sedation produced by barbiturates. In addition it stimulates the reticular formation of the medulla of certain animals. Rinaldi and Himwich[5] have suggested that this action is the basis of the parkinsonian-like tremor which is sometimes produced in man. Reserpine has also been shown to lower the threshold for convulsive seizures,[6] thus increasing the frequency of fits in epileptics[7] and to be antagonistic to phenytoin.[8]

Although it has been widely used, and in large doses, in mental hospitals for its tranquillizing effect, reserpine can cause severe depression, agitation and psychosis in hypertensive patients on long-term treatment.

There is ample evidence to suggest that the blood-pressure-lowering effect of reserpine is of central origin. However, it is obvious that any hypotensive drug must produce its ultimate effect either by diminishing the force of cardiac contraction and cardiac output or by reducing the peripheral resistance. In dogs, cardiac output is not decreased to any significant extent after the administration of reserpine[9] and the fall in blood pressure is due to a decrease in the peripheral resistance.

Reserpine appears to produce its effect by damping down the afferent impulses reaching the medulla and thus reflexly diminishing the central sympathetic outflow.[10] It is well established that inhibition of central vasoconstrictor impulses can effectively reduce peripheral resistance and cause lowering of the blood pressure. Depression of sympathetic activity leads to overaction of the parasympathetic nervous system, thus producing myosis, bradycardia and diarrhoea, which was first observed by Bein[11] to occur after the administration of reserpine.

Authors' Investigations

A. Acute Experiments

The effect of intravenous injection of reserpine on blood pressure and peripheral blood flow.

Reserpine* was given by single or repeated intravenous injection to 10 patients, 2 of whom had severe hypertension, 2 were cases of mild hypertension, 4 had a recurrence of hypertension after a lumbo-dorsal splanchnicectomy (Smithwick operation), 1 had had all four limbs sympathectomized for Raynaud's disease, and 1 had had a unilateral lumbar sympathectomy for varicose ulceration. Continuous records were obtained of the peripheral circulation by means of the optical digital plethysmograph described in detail elsewhere.[12-14] This sensitive method not only allows correct registration of the height of the pulse volume of two digits simultaneously, but also permits calculation of the arterial inflow by means of the venous-congestion test. The blood pressure was taken at regular intervals by clinical methods and the heart rate was, of course, available from the plethysmographic records. Only those 'Smithwick' patients were selected in whom the operation had included removal of the first and second lumbar ganglia, i.e. the lower limbs had been sympathectomized. All were examined for sympathetic activity in the lower extremities to ascertain that the sympathectomy was complete. As at Groote Schuur Hospital, at one time, sympathectomy had been extended to include the thoracic chain up to D_2,[15] the hands were examined as well to ascertain whether the vessels of the hands were under full sympathetic control.

Fig. 1. demonstrates such a preliminary test in the patient whose response to reserpine is shown in Fig. 4. After body heating by immersion of one upper limb in water at 45°C there is marked reflex vasodilatation of the other upper limb, due to the release of sympathetic tone. In the lower (sympathectomized) extremities, however, a decrease in pulse volume is recorded.

As has previously been demonstrated[12] this is typical of a sympathectomized limb and is due to shunting of blood away from the sympathectomized limb to other vascular beds which respond with reflex dilatation. The sympathectomized vessels respond to local heating with dilatation, indicating that the failure to respond to reflex heating was not due to organic changes. In addition, absence of thermoregulatory sweating was observed in the lower limbs of all 'Smithwick' patients. Similar tests were carried out in the patient who had had all four limbs sympathectomized for Raynaud's disease and in the patient who had had a unilateral lumbar sympathectomy. They showed conclusively that

* We gratefully acknowledge the supply of 'Serpiloid', a pure reserpine preparation, by Riker Laboratories, Port Elizabeth.

TABLE I. EFFECT ON BLOOD PRESSURE AND PULSE VOLUME OF INTRAVENOUS INJECTION OF RESERPINE

Patient	*Average Resting Blood Pressure*	*Dose*	*How given intravenously*	*Average Final Blood Pressure*	*Fall in Blood Pressure*	*Pulse Volume*		*Remarks*
						Normal Digit	*Sympathectomized Digit*	
1	225/118	1·5 mg.	1 dose	230/105	25/13	Finger: gradual dilatation Toe: gradual dilatation		The gradual increase in pulse volume observed in these cases is commonly seen on prolonged rest and is due to release of sympathetic tone.
2	230/128	2 mg.	1 dose	206/118	24/10	Finger: slight dilatation Toe: gradual dilatation		
3	172/126	4 mg.	4×1 mg.	154/100	22/26	Finger: slight dilatation Toe: gradual dilatation		
4	172/88	2·5 mg.	2×1 mg. 1×0·5 mg.	164/80	8/8	Finger: unchanged Toe: gradual dilatation		
5	245/145	1·5 mg.	1 dose	110/80	135/65	Finger: slight dilatation	Toe: marked fairly rapid dilation	Previous Smithwick operation
6	230/155	2 mg.	2×1 mg.	160/122	70/33	Finger: constriction	Toe: marked fairly rapid dilatation	Previous Smithwick operation
7	230/124	3 mg.	3×1 mg.	112/74	118/50	Finger: slight dilatation	Toe: marked rapid dilatation	Previous Smithwick operation
8	245/150	1 mg.	1 dose	228/128	17/22	Finger: gradual dilatation	Toe: gradual dilatation	Previous Smithwick operation. Fall in blood pressure very slight; possibly due to small dose of reserpine administered
9	142/74	2 mg.	1 dose	116/63	22/11		Finger: marked very rapid dilatation Toe: marked very rapid dilatation	All four limbs sympathectomized for Raynaud's disease
10	118/76	2 mg.	1 dose	110/64	8/12	Right toe: Unchanged	Left toe: marked dilatation	Unilateral lumbar sympathectomy for varicose ulcer

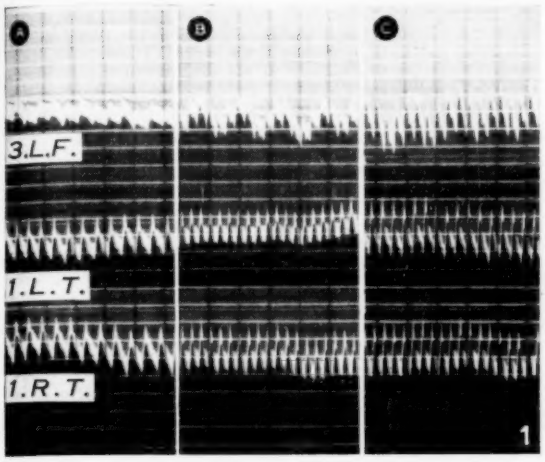

Fig. 1. Pulse volume of the third left finger (3.L.F.), first left toe (1.L.T.) and first right toe (1.R.T.) in a patient who had previously undergone a lumbo-dorsal splanchnicectomy for hypertension.

A. Before body heating. B. After body heating. Note the increase in pulse volume of the finger and the decrease in the toes, demonstrating that the vessels of the finger are under normal sympathetic tone, whereas those of the toes are sympathectomized. C. Response to local application of heat. Note particularly the increase in the pulse volume of the toes indicating that the failure to respond to body heating was not due to organic arterial disease of the vessels.

the sympathectomies were complete and that there was no organic vascular occlusion.

Results

The results are summarized in Table I. They differed both as regards peripheral vascular and hypotensive effect, according to whether the sympathetic vasomotor supply was 'normal' or had been interrupted. Whereas the intravenous injection of reserpine produces a marked and relatively rapid vasodilator effect on sympathectomized blood vessels, its effect in the non-sympathectomized extremity is uncertain (Fig. 2) and when vasodilatation takes place it is slow and delayed (Fig. 3C). Lower and upper extremities also seem

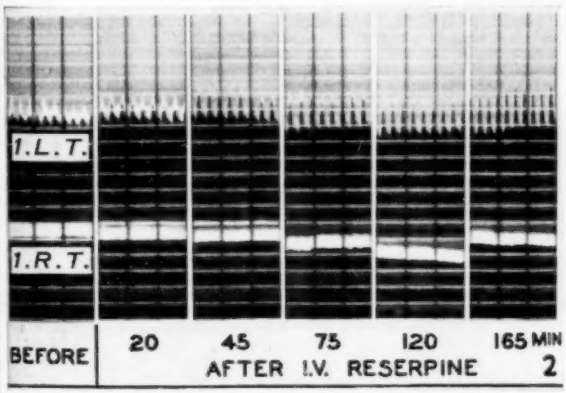

Fig. 2. Effect of 2 mg. of intravenous reserpine on blood flow of first left toe (1.L.T.) and first right toe (1.R.T.) in a patient who has had a left lumbar sympathectomy for varicose ulcers. Tracings recorded before and after injection at times indicated. Note the marked vasodilatation of the sympathectomized vessels (1.L.T.), whereas there was no change in pulse volume of the non-sympathectomized vessels (1.R.T.).

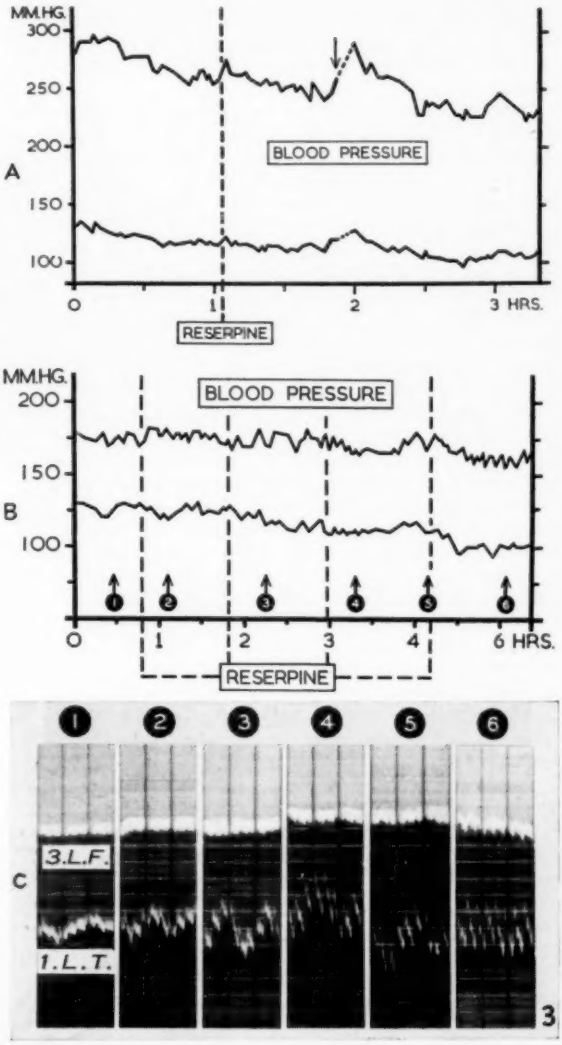

Fig. 3. The effect of intravenous reserpine.

A. In a patient with severe hypertension. Note the rise in blood pressure following the ingestion of a light meal (indicated by the arrow). B. In a patient with mild hypertension. Note the slight fall in blood pressure in A and B as compared with the dramatic response shown in Fig. 4. C. Effect on peripheral blood flow of upper (3.L.F.) and lower (1.L.T.) extremities in a patient whose blood pressure response was seen in Fig. 3B. The tracings of the pulse volume were recorded at the points numbered in the diagram. Note the marked difference in the response between upper and lower extremities. The gradual dilatation obtained in the lower extremities was considered to be the effect of rest rather than that due to the drug.

to differ in their response inasmuch as vasodilatation is more definite in the upper. This is well illustrated by Fig. 3C and the data were the same in both mild and severe hypertensives.

Towards the end of the test two patients exhibited marked flushing of the face, were sleepy, frequently yawned, and developed conjunctival injection. There was, however, no nasal congestion. Despite the fact that the 'normal' hypertensive patients received large amounts of reserpine the fall in blood pressure was quite unimpressive and was of the same order as might be expected to occur after prolonged rest and mild sedation (Fig. 3A and 3B).

This was in marked contrast to the behaviour of the blood pressure in patients who had undergone Smithwick operations but in whom the hypertension had recurred. Three of the four patients tested received a dose of reserpine that was of the same order as that administered to the 'normal' patients (or slightly smaller). The drop in blood pressure was profound and greatly exceeded that obtained in the latter. Moreover, the fall was rapid and occurred simultaneously with a marked vasodilatation in the sympathectomized lower extremities, usually commencing within 30 minutes of an adequate injection. Fig. 4 illustrates such a case. As the plethysmogram of the normal finger registered spontaneous fluctuations it is to be concluded that such ablation of central vasomotor activity as is said to occur

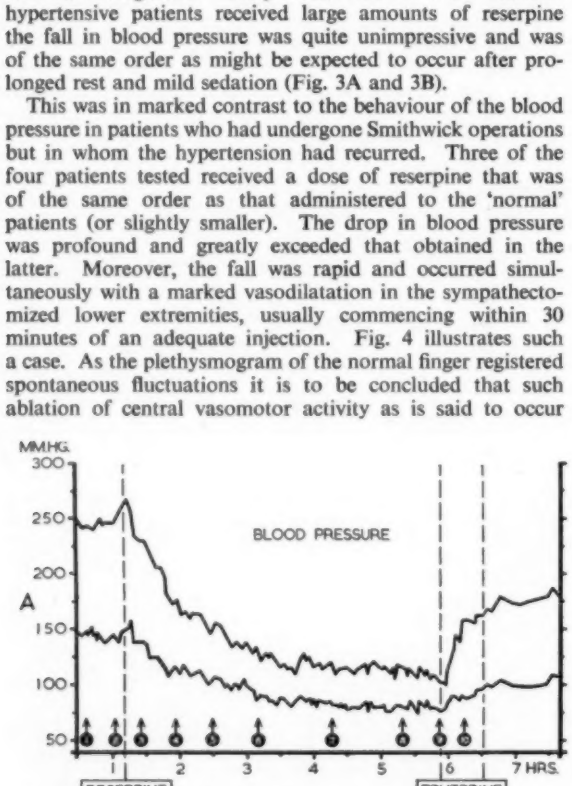

Fig. 4. Effect of 1·5 mg. intravenous reserpine on blood pressure and blood flow of third left finger (3.L.F.) and first left toe (1.L.T.) in a patient who has had a lumbo-dorsal splanchnicectomy (same patient as Fig. 1). Tracing of pulse volume recorded at the points indicated by numbers on the diagram of blood pressure. Note the pronounced fall in blood pressure which was associated with marked vasodilatation in the sympathectomized vessels (1.L.T.). There was some vasodilatation in the non-sympathectomized digit (3.L.F.) as well. To combat fall in blood pressure 1 gr. of ephedrine was given subcutaneously, followed by ½ gr. by mouth.

with reserpine did not entirely abolish reflex vasomotor activity in the peripheral vessels. Being sympathectomized, the vessels of the lower extremities were not affected by this vasomotor activity and, irrespective of the reaction in the upper limb, proceeded to dilate. This lends support to the contention that the dilatation of the sympathectomized vessels in the lower extremities is due to a local effect on the vessel itself.

Pallor of the face was marked in all three cases and shivering, sweating, diarrhoea and angina were also encountered. It was not possible to ascertain whether the pallor was due to active vasoconstriction, occurring in an attempt to maintain the blood pressure, or was due to a postural effect, since all tests were carried out with the patient sitting.

The profound hypotension caused by a single intravenous injection of reserpine in the 'Smithwick' patients responded to subcutaneous injection of ephedrine (Fig. 4). In fact, ephedrine was given in such cases when the drop produced by reserpine caused untoward systemic effects. The hypotension induced by these tests lasted for several hours, and at the next attendance at the hospital a few days later the blood pressure had always risen to almost pre-treatment levels. The degree of hypotension observed in the acute experiment could never be achieved by administering rauwolfia or reserpine by mouth, even if given over a prolonged period.

One of our 'Smithwick' patients responded like the 'normal' hypertensives with a gradual, delayed but marked vasodilatation in both upper and lower limbs and face, unaccompanied by anything but a very minor and insignificant fall in blood pressure. The reason for this different response is not clear; possibly it was related to the fact that the dose of reserpine administered was considerably smaller (1 mg.) than in the other 'Smithwick' patients, who received 1·5-3 mg.

In the patient who had sympathectomies of all 4 limbs, both the upper and the lower extremities responded like the sympathectomized limbs of our 'Smithwick' patients, with a marked and rapid vasodilatation. This was accompanied by marked flushing of the face. However, the fall in blood pressure produced was very slight and was of the same order as that which occurred in the non-sympathectomized patients.

A similar result was obtained in the patient who had had a unilateral lumbar sympathectomy. Marked vasodilatation occurred in the sympathectomized digit, whereas there was no change in pulse volume in the other non-sympathectomized toe (Fig. 2).

This test demonstrated very clearly the uncertainty of the peripheral vascular effect of reserpine on non-sympathectomized vessels. As might be expected in a normotensive patient, the fall in blood pressure was unimpressive.

Discussion

From these results it appears that in man intravenous reserpine has a definite vasodilator effect on sympathectomized blood vessels. This effect must of necessity be a local one on the wall of the vessel itself, unless one postulates stimulation of vasodilator fibres which do not run with the sympathetic, a concept which has not found any acceptance.

This vasodilatation is contrary to observations by McQueen *et al.*[16] to the effect that intraperitoneal reserpine markedly

dilates the non-sympathectomized vessels, but results either in no change or in a decrease in the diameter of the blood vessels of the sympathectomized rabbit's ear. This suggested to McQueen and his colleagues that peripheral vasodilatation is dependent upon the integrity of the peripheral sympathetic nervous system. Quite apart from the fact that it cannot be assumed that results obtained in other species are valid in man, failure of the sympathectomized vessels to dilate might in their experiments have been caused by a shunting of blood into other areas, particularly as a marked general vasodilatation was obtained. Such shunting would have been potentiated if in addition there was a fall in blood pressure, however small.

The vasodilatation obtained in the digital vessels of the 'normal' patients and in the vessels of the upper limbs in some of the 'Smithwick' patients was due to release of central vasomotor tone. Such release is commonly seen on prolonged rest alone, and it cannot with any certainty be ascribed to a central effect of reserpine.

The question of the cause of the pronounced hypotensive effect of reserpine in 'Smithwick' patients is very pertinent. It is generally assumed that the hypotensive effect of reserpine is due to a central inhibition of reflex vasomotor tone. This, however, can no longer be effective in the splanchnicectomized patient and we have to look for a different mechanism. We have shown that in man reserpine has a powerful dilator effect on the sympathectomized vessels of the extremities. There is nothing to militate against the assumption that it has the same action on the sympathectomized splanchnic vessels, which will result in a marked reduction of peripheral resistance and a drop in blood pressure. This concept is supported by the effect of reserpine in the patient who had all four limbs sympathectomized, but whose splanchnic bed was under normal sympathetic control. Marked peripheral vasodilatation was obtained, but was unaccompanied by any significant fall in blood pressure, owing to the fact that the sympathectomized area was small compared with the normal splanchnic bed. It underlines the well-known fact that vasodilatation of the limb vessels alone does not produce a significant drop in blood pressure.

B. CLINICAL ASPECT

Whereas in the experimental field reserpine has been used almost exclusively, all the preparations listed above have been employed in the treatment of hypertension. Although most authors have confined their investigations to one particular rauwolfia preparation, there are some who compared one or more in different groups of patients. Achor *et al.*,[17] for instance, found no difference in the therapeutic action or side-effects between a whole-root preparation and reserpine. Similarly Locket[4] did not detect any difference between a whole-root extract and the alseroxylon fraction, and Moyer *et al.*[18] found that Roxinil had similar actions as the alseroxylon fraction and reserpine. Having compared all the above-mentioned preparations with Rescinnamine, Moyer *et al.*[3] came to the conclusion that there was not much to choose between the five preparations as regards hypotensive effect and the incidence of side-effects. The severity, however, of side-effects, including depressive reactions, was most marked in the patients treated with reserpine.

Side-effects and toxic reactions of reserpine have received the greatest publicity, but whether this is due to the large number of patients treated with this preparation, or whether it is a true index of greater toxicity as Moyer *et al.*[3] suggest, remains to be confirmed.

That *Rauwolfia serpentina* is not the whole answer to the treatment of hypertension has been abundantly demonstrated by the number of authors who have been forced to combine it with other drugs. The combination most widely used and generally accepted as the best treatment for severe hypertension, is pentapyrrolidinium and a rauwolfia preparation, usually reserpine.[19-21] This combination has proved more potent than either drug alone, thus causing fewer side-effects. Moreover, a more sustained hypotensive effect is obtained than if pentapyrrolidinium is used alone. The results have been more controversial when *Veratrum viride* or hydralizine was combined with rauwolfia.

Whereas there seems little to choose between the various rauwolfia preparations, the question which type of patient will respond best to treatment, and the degree of hypotension to be expected in the individual patient, is more difficult to answer. In our clinic we see a large number of patients with arteriosclerosis complicated by hypertension where treatment presents a special problem owing to complications such as cerebro-vascular accidents, and in whom the indications for hypotensive drugs are by no means unquestioned. We also see cases who have been treated in the past by lumbo-dorsal splanchnicectomy and in whom hypertension has recurred. Little has been found in the literature about the use of hypotensive drugs in the latter group. It is also by no means settled whether the response is different in mild, as opposed to severe, cases of hypertension. We have therefore instituted investigations into these two groups of patients, viz. (*a*) patients with long-standing hypertension associated with advanced arteriosclerosis affecting coronary, renal, cerebral and peripheral vessels, who had responded poorly to treatment in the past, and (*b*) cases whose hypertension recurred after lumbo-dorsal sympathectomy. The average blood pressure of group (*b*) before treatment was 238/141 mm. Hg. Only one of all the patients had normal fundi and all but one had evidence of left ventricular hypertrophy.

All patients were seen by special appointment first at weekly intervals, and later fortnightly. Blood-pressure readings were taken after a period of rest of 15-20 minutes. Some of the hypotensive drugs produce postural hypotension and the position of the patient at the time of reading the blood pressure was important. In fact, pressure readings with the patient lying down may bear very little resemblance to the pressure in the ambulant patient and may be very misleading as regards the efficacy of the treatment under review. We therefore measured the blood pressure at half-minute intervals first in the recumbent and then in the erect posture. A minimum of 6 readings and a maximum of 10 were taken in each position. From these figures an average blood-pressure reading for both positions was obtained at every attendance. The pulse rate was taken at the end of each series of blood-pressure recordings.

Before treatment was begun, a full investigation of each patient was made, including a detailed history, physical examination, examination of fundi, urinalysis, blood urea, electrocardiogram, X-ray of chest, phenolsulphonphthalein (PSP) excretion test. Patients were seen on several occasions before the commencement of treatment.

The patients were first given Rauwiloid and, according to the effect on the blood pressure, Veriloid* was subsequently added. The dosage of this was cautiously increased until either a satisfactory hypotensive effect was obtained or nausea and vomiting precluded a further increase in dosage. If the reduction was still unsatisfactory, pentolinium was added.

For the purpose of evaluating the results, the following scheme of grading was adopted. Irrespective of the height of the initial blood pressure a fall of 30 mm. Hg in systolic blood pressure, in either the lying posture or the standing, was considered a 'good' response. A fall in blood pressure between 20 and 30 mm. Hg was charted as 'moderate' and smaller changes as 'no' response.

(*a*) *Effect on Blood Pressure*

Of the 20 patients treated with Rauwiloid, 6 responded inadequately within 6-12 weeks' treatment and it was felt

TABLE II. BLOOD-PRESSURE RESPONSE IN PATIENTS WITH RAUWILOID OR RAUWILOID + VERILOID

Drug Used	*No. of Patients*	*Good Response (Fall over 30 mm. Hg)*		*Moderate Response (Fall over 20 mm. Hg)*		*No Response (Fall under 20 mm. Hg)*	
		No.	*%*	*No.*	*%*	*No.*	*%*
Rauwiloid	20	9	45	5	25	6	30
Rauwiloid or Rauwiloid + Veriloid ..	22	10	45	5	23	7	32

unjustifiable to withhold other drugs, which were accordingly added. The rest of the patients were treated from 4-6 months.

Of the 20 patients who received Rauwiloid only, 9 (45%) showed a good response, the average fall in blood pressure being 38 mm. Hg in the lying position and 36 mm. Hg in the standing. The response was moderate in 5 (25%), the average fall being 21·4 mm. Hg in the lying position and 20·8 in the standing. Rauwiloid had no effect in 6 patients (30%)—Table II.

Because there had been little or no response to treatment with Rauwiloid alone, or because a further fall in blood pressure seemed desirable, 6 patients were in addition treated with Veriloid. In only one did the addition of Veriloid lower the blood pressure sufficiently to upgrade this patient from the 'moderate' into the 'good' response group, and those patients who had not responded to treatment with Rauwiloid alone also did not respond after Veriloid had been added. In fact, the average fall in blood pressure after treatment with Rauwiloid was practically identical with that obtained after additional treatment with Veriloid or after treatment with Rauwiloid and Veriloid from the start.

We therefore concluded that there was very little to be gained by the additional administration of Veriloid to patients who were already treated with Rauwiloid. Moreover, Veriloid produced vomiting in most patients at one stage or another during treatment and the dosage had to be adjusted accordingly. In 3 patients vomiting proved troublesome and necessitated the cessation of treatment.

(*b*) *Height of the Initial Blood Pressure in Relation to the Therapeutic Response*

The question arose whether the height of the blood pressure had any relation to the response to be expected. It was found that the patients who responded best had an average blood pressure of 203/117 mm. Hg, those who responded moderately well a blood pressure of 214/131 mm. Hg, and those who did not respond at all the highest average pressures, namely 223/133 mm. Hg (Table III). Our results, therefore, agree with other authors, who found that a larger percentage of patients with mild hypertension responded to treatment and that a higher percentage of failures is seen in the more severe type.

TABLE III. INITIAL BLOOD PRESSURE IN RELATION TO THERAPEUTIC RESPONSE IN 22 PATIENTS TREATED WITH RAUWILOID OR RAUWILOID + VERILOID

B.P. Response	*No. of Patients*	*Percentage of Total*	*Initial B.P.*
Fall of over 30 mm. Hg	10	45	203/117
Fall of over 20 mm. Hg	5	23	214/131
Fall of under 20 mm. Hg	7	32	223/133

Whereas this holds good for groups of patients, in the individual patient the result cannot be predicted. This is very clearly demonstrated if all the patients are divided into two groups, viz. (*a*) those with an initial diastolic blood pressure above 120 mm. Hg, and (*b*) those with an initial diastolic blood pressure below 120 mm. Hg. In Table IV it will be seen that of the patients with the higher diastolic pressures 25% responded well (fall in diastolic blood pressure of more than 30 mm. Hg) and 42% failed to respond, as against 70% and 20% respectively in those patients whose diastolic blood pressure was below 120 mm. Hg. The average fall in blood pressure of the severe hypertensive who reacted was, however, much greater than in the milder cases; that is to say, if a severe hypertensive does respond well to Rauwiloid the actual fall in blood pressure will easily exceed anything seen in the moderate group. It is because of this excellent response in the few cases with severe hypertension that the average fall in blood pressure in the severe group as a whole is slightly better than the average fall in blood pressure of the mild group. It would thus be misleading to consider only the averages. It will also be seen from Table IV that a relatively large percentage of patients with an initial diastolic pressure of above 120 mm. Hg exhibited moderate response. However, it must be realized that a fall in blood pressure of 20-30 mm. Hg systolic in a patient with severe hypertension constitutes a poor therapeutic response, whereas an equivalent fall in mild hypertension represents a satisfactory therapeutic result.

TABLE IV. THERAPEUTIC RESPONSE ACCORDING TO INITIAL DIASTOLIC BLOOD PRESSURE PATIENTS TREATED WITH RAUWILOID OR RAUWILOID + VERILOID

Therapeutic Response	*Initial Diastolic B.P. above 120 mm. Hg*			*Initial Diastolic B.P. below 120 mm. Hg*		
	No.	*%*	*Av. fall B.P.*	*No.*	*%*	*Av. fall B.P.*
Good	3	25	42/30	7	70	34/17
Moderate	4	33	21/13	1	10	21/18
Nil	5	42	5/10	2	20	8/10
Total	12	100	23/15	10	100	12/12

(*c*) *Results in Hypertensive Patients who have undergone a Lumbo-Dorsal Splanchnicectomy (Smithwick operation)*

In view of the fact that a marked fall in blood pressure could be produced in this group of patients by the intravenous injection of reserpine in the acute experiments, the results of long-term oral therapy with Rauwiloid tablets were of

* A compound tablet consisting of 1 mg. of Rauwiloid and 3 mg. of *Veratrum viride*.

TABLE V. COMPARISON OF RESULTS IN PATIENTS WHO HAVE AND WHO HAVE NOT HAD A PREVIOUS SMITHWICK OPERATION

	'Smithwick' Patients	*'Non-Smithwick' Patients*
No. of patients	8	14
Initial B.P.	238/141*	198/116*
	218/135†	193/118†
Fall of over 30 mm. Hg	2 (25%)	8 (57%)
Fall of over 20 mm. Hg	2 (25%)	3 (21·5%)
Fall of under 20 mm. Hg	4 (50%)	3 (21·5%)

* Lying. † Standing.

considerable interest. The fact that the therapeutic response in these patients was much worse than in the 'normal' patients came as a surprise. In Table V it will be seen that of the 'Smithwick' patients only 2 (25%) responded well, 2 (25%) moderately, and 4 (50%) not at all.

It must be pointed out that the average blood pressure in the 'Smithwick' patients before treatment was 238/141 mm. Hg lying and 218/135 standing, whereas in the 'non-Smithwick' group the blood pressure was 198/116 lying and 193/118 standing. In the light of what has been said above, the response is probably a reflection of the difference in the initial height of the blood pressure in the two groups.

(*d*) *Effect of Reserpine*

Since it has been claimed that reserpine, has a greater therapeutic effect than other rauwolfia preparations, the effect of the pure alkaloid (Serpasil, 1·25 mg. per day) was tried on 7 patients to see whether a further fall in blood pressure could be produced.

There was no essential difference in the recumbent blood pressure in any of the patients when reserpine was added, irrespective of whether they had been treated with Rauwiloid, or with a combination of Rauwiloid and Veriloid and Ansolysen. In 2 patients, however, there was a slight fall in the standing blood pressure. In contrast to the doubtful therapeutic response, we encountered one definite toxic reaction in a patient who had tolerated 4 mg. of Rauwiloid per day for 1 year, without any trouble. After only 1 week of treatment he developed nervousness, insomnia and depression with brooding thoughts and fear of impending death.

We, therefore, felt that not only was there no additional advantage in giving reserpine, but that it produced nervousness and depression which had been absent even on prolonged treatment with Rauwiloid.

(*e*) *Effect on Symptoms other than Blood Pressure*

Angina. A most gratifying result was obtained in 4 patients who had angina before treatment commenced. There was marked improvement in 2 and some improvement in the other 2 patients. One patient, who had been practically incapacitated by very frequent attacks of angina and a severe shoulder-hand syndrome, on treatment with Rauwiloid experienced marked relief, the frequency of attacks decreasing from about 15 to 1 or 2 per day. At the same time physiotherapy became more effective and resulted in almost complete relief of her shoulder-hand syndrome. In another patient the frequency of the attacks was reduced from 3-4 per day to 2-3 per week. In the other 2 patients, who had less frequent attacks of angina before commencing treatment, there was a definite improvement both in the severity and number of attacks, but not complete relief.

Intermittent Claudication. Six patients complained of intermittent claudication. There was very slight improvement in 3 and none in the other 3.

Postural Hypotension. This was an interesting side-effect noted in 3 'Smithwick' patients, who had had this symptom in a mild degree before the commencement of therapy. Only one of these belonged to the 'good response' group and in her the hypotension was so marked that she fainted one morning. The other two had only responded with a moderate fall in blood pressure and it is of interest to note that a relatively small drop in blood pressure produced a marked increase in postural hypotensive symptoms.

Complications. Congestion of the air passages and sleepiness were mentioned by one or two patients, but never proved troublesome symptoms.

Myocardial Infarction. Two patients developed myocardial infarction while under treatment. One of these had had 2 attacks of angina at rest before the commencement of treatment. In his case the infarction occurred after an episode of severe vomiting induced by Veriloid, and the resultant dehydration might well have been a predisposing factor in the production of a coronary thrombosis. The blood-pressure readings a few days before the infarction had not been particularly low. The other patient had a typical history of a previous infarction 8 years before, but without any residual changes in the electrocardiogram. A third patient developed an extension of an old posterior myocardial infarction. In both these latter cases the exact time of the infarction is not known, and there had been no episodes of marked hypotension. This relatively high incidence of cardiac complications is a reflection of the type of case treated rather than the result of therapy.

Mental Depression. This has been mentioned frequently in the literature as one of the serious side-effects of Rauwolfia therapy. In our series mental depression, bordering on mild psychosis, was recorded in only one patient, who had been treated with Rauwiloid for 5 months, the dose during the last 2 months having been increased from 8 mg. per day to 12 mg. per day. This man became extremely nervous, restless, anxious and somewhat agitated and also developed attacks of 'shakiness and tremors', which cleared up 2-3 weeks after Rauwiloid was withdrawn. In 3 other patients attacks were encountered which were variously described as 'shaking' or 'shivering', and were frequently associated with a feeling of nervousness and unrest. In every case the attacks ceased after Rauwiloid was stopped or the dose reduced. All but one of these 4 patients had been on large doses of Rauwiloid (12 mg. per day) for some considerable time, and 3 of them were extremely nervous and apprehensive individuals. One other patient was unusually sensitive to the drug. She developed insomnia, nervousness, tremor, arthralgia and joint stiffness, necessitating withdrawal of the drug after only 2 weeks' treatment.

DISCUSSION

Whereas there is considerable divergence in opinion on the results of treatment of mild hypertension with Rauwolfia alkaloids, the percentage response reported varying from 25%[19] to 100%[22] in different series, it would appear from the literature that patients with fixed hypertension and arteriosclerosis respond less well to hypotensive drugs than those with the early and labile type.[23,24] Our results are

quite compatible with this view. Examining a series of long-standing cases of hypertension with marked arteriosclerosis, we obtained a good response in 45% of cases, a moderate response in 23% and no response in 32%.

It has been stated that severe cases with symptoms frequently respond better than milder cases.[4] We agree with that view only in so far that if a patient with severe hypertension responds to treatment the fall in blood pressure is commonly greater than the drop obtained in a patient with mild hypertension. In our group of patients the percentage of good responses was much greater in the mild cases than in the severe ones. This was brought out very clearly when we divided our cases into those with diastolic pressures above and below 120 mm. Hg. Only 25% of the former showed a good response as opposed to 70% of the latter. In this our results differ from those of McGregor and Segel[25] and Moyer,[26] who found Rauwolfia equally effective in both mild and severe cases, and from those of Platt and Sears[27] who obtained a 'significant and sometimes profound effect in at least 40% of cases' all of whom had severe hypertension.

Although in the acute experiment an excellent hypotensive effect was obtained with reserpine in 'Smithwick' patients, on prolonged oral therapy these patients behaved in exactly the same way as all other patients with severe hypertension.

Our patients who had been on an adequate dose of Rauwiloid have not derived any benefit when Veriloid or Serpasil were added in an attempt to obtain a further fall in blood pressure. The results obtained with Rauwiloid alone were the same as with any other combination administered in these investigations. The difficulties and complications encountered in the administration of Veriloid far outweighed its therapeutic value. It must be admitted, however, that all our patients had been treated first with Rauwiloid and that the results may have been different had treatment been commenced with veratrum and Rauwiloid added subsequently.

Severe mental depression occurred in only one of our patients, but 3 others complained of nervousness, shakiness and unrest and one of these also developed arthralgia.

Unlike Smirk and McQueen's patients,[28] who were treated with reserpine, none of our patients needed psychiatric treatment and all toxic symptoms spontaneously cleared up after cessation of therapy. We also have evidence in one case that reserpine is more toxic than the alseroxylon fraction —a similar observation to that previously reported on the comparison of reserpine and rescinnamine.[23]

We would agree that with a higher dosage of Rauwiloid toxic reactions are more liable to occur.[4] However, 2 of our patients developed nervousness, tremor and anxiety when on only 4 mg. of Rauwiloid per day.

The alseroxylon fraction is, therefore, by no means without its unpleasant side-effects, although they are probably less severe than those encountered with reserpine.

SUMMARY AND CONCLUSION

The effect of intravenous reserpine on peripheral blood flow and blood pressure was investigated in a group of 'normal' hypertensive patients and compared with a group of hypertensives who had previously undergone a lumbo-dorsal splanchnicectomy.

It was shown that the hypotensive effect was much larger in the latter group, and this was thought to be related to the marked vasodilator action which intravenous reserpine has on sympathectomized blood vessels.

Vasodilatation was only associated with a dramatic fall in blood pressure if the sympathectomized vascular bed was large enough, i.e. if the splanchnic bed was sympathectomized as well. The hypotensive effect was transient, and comparable low blood-pressure levels could not be maintained by oral administration in the same 'Smithwick' patients.

The effect of reserpine on the non-sympathectomized vessels was unpredictable and did not bear any constant relation to the moderate drop in blood pressure obtained.

On long-term treatment with Rauwiloid there was no difference in the therapeutic response between the 'normal' and the sympathectomized hypertensive patients, and Rauwiloid was found useful in 45% of cases.

We could arrive at no conclusion as to which case would respond best to treatment although, as might be expected, a bigger fall in blood pressure was obtained in patients with a more severe hypertension but a larger percentage of the milder cases responded to treatment.

Rauwiloid produced unpleasant side-effects in 22% of cases.

In our series the addition of Veriloid was of very little benefit and certainly did not justify the amount of time and trouble spent in stabilization both for the patient and the physician.

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OPERATIVE CHOLANGIOGRAPHY*

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This study is based on 140 consecutive cases under my care of disease involving the biliary tract, operated on between October 1955 and March 1957. Operative cholangiography was performed in all cases. In addition, control or/and post-operative cholangiograms were taken in a further 12 cases, where operative X-ray was not found necessary.

Cholangiography at operation does not replace routine search for common-duct stones, and does not ignore the accepted indications for exploration of the common duct, which are the following:

1. History of, or presence of jaundice.
2. Dilatation of the common duct.
3. 'Gravel' in gall-bladder, with wide cystic duct.
4. Positive findings on palpation of common duct or pancreas.
5. Contracted gall-bladder, with wide common duct.

We have not used cholangio-manometry or the cholelithophone or the recently described biliary endoscope. Possibly pressure studies may be of value in cases of biliary colic in the absence of any obvious pathological condition ('dyskinesia').

TECHNIQUE

1. A suitable wooden tunnel for taking a 12 × 15 inch X-ray cassette is placed on the operating table in the required position.

2. A 12×15 inch cassette with stationary grid strapped on is slipped into the tunnel. The patient is positioned so that the right twelfth rib is in the middle of the cassette. The patient is rotated slightly onto his right side so as to project the bile ducts clear of the spine.

3. Laparotomy is performed, and all abdominal and pelvic organs palpated.

4. Dissection begins at the gall-bladder neck and the cystic duct is positively identified. The cystic artery is tied and divided at this stage if it can be identified. Two silk ligatures are passed round the cystic duct; the one nearer the gall-bladder is tied and the other kept loose. An opening is cut into the cystic duct between the ligatures. (If there is any difficulty in identifying the cystic duct, cholecystectomy proceeds from the fundus downwards, and only then, when the duct is identified, is cholangiography carried out.)

Meanwhile 20 c.c. of 35% Pyelosil has been drawn into a syringe, and an 8-inch length of polythene tubing attached *via* a well-fitting needle. Air-bubbles are excluded and the end of the tube is now threaded into the cystic duct, the silk ligature being tied firmly over it.

5. All metal clips and instruments are removed, the X-ray apparatus wheeled into position, the dye injected and the exposure made. The anaesthetist provides for cessation of respiration by hyperventilation. (*Note:* a non-explosive anaesthetic must be used when radiographs are taken in the operating-room.)

6. Cholecystectomy is completed.

7. The common duct and the head of the pancreas are again inspected and palpated, and a decision regarding exploration of the common duct is tentatively made. By this time the X-ray plate is back for inspection, and is a further help towards this decision.

8. A normal cholangiogram (Fig. 1) shows a filled biliary tree with smooth contours and undilated, free flow of dye into duodenum, and no filling defects. The operation is completed if such is the case.

9. If an abnormality exists calling for opening of the common duct (Fig. 2), the operation proceeds in the usual manner, a T-tube is sewn in watertight, and a *control* cholangiogram is taken at this stage, again taking care to eliminate air-bubbles by a preliminary saline flush.

10. A routine post-operative cholangiogram is made on the 14th day in cases where a T-tube had been inserted (Fig. 3).

VARIATIONS OF TECHNIQUE

1. Cholecysto-cholangiography *via* a Foley catheter in the gall-bladder, used in cases of 'dyskinesia', and in association with manometry.

2. Direct injection of dye into the common duct by needle and syringe, used in post-cholecystectomy cases, and in cases where the ductal anatomy cannot be absolutely identified.

3. Frequently removal of the gall-bladder has to proceed from the fundus downwards; only after the cystic duct has been absolutely identified can the cholangiogram be taken.

4. Where the common duct is dilated, a larger amount of dye should be used, but it is wise to make one exposure after injecting 10 c.c. only, and another after injecting a further 10-20 c.c. This reduces the possibility that stones may be obscured by overfilling of the duct with dye.

5. When stones are palpated in the common duct, a primary cholangiogram is not required, but *control* at the end of the procedure is of great importance.

6. In common-duct strictures, the intra-hepatic biliary tree

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Fig. 1. Normal operative cholangiogram. *Fig.* 2. Multiple common-duct stones. *Fig.* 3. Normal post-operative cholangiogram. *Fig.* 4. Main pancreatic duct demonstrated. *Fig.* 5. Retained common-duct stone after operation elsewhere. *Fig.* 6. Cholecystocholangiogram showing anomaly of cystic duct entering duodenum at ampulla of Vater. *Fig.* 7. 'False negative'. Overfilled common duct fails to show 8 small stones. *Fig.* 8. Stones in common duct. *No* history of jaundice. Stones *not* palpable at operation. *Fig.* 9. Post-cholecystectomy syndrome. Stone in common duct (A) as well as large cystic-duct stump (B), containing stones.

frequently contains stones. Cholangiography is useful to confirm and control adequate removal.

DANGERS AND COMPLICATIONS

Only in one case have we experienced considerable bile leakage from needle-puncture of the common duct. No other complications have occurred. The following have been described:

1. Pancreatitis. This will only occur if sufficient pressure is used to rupture intrapancreatic ducts.
2. Cholangitis or liver damage due to the contrast medium or infection.
3. Sensitivity to iodine.
4. Radiation danger to personnel. This is negligible if members of the operating team stand well back from the table during the exposure.
5. Bile leakage from common-duct needle-puncture may be considerable. Drainage should always be provided.

RESULTS

Tables I-V indicate the more important findings in the present investigation.

TABLE I. NUMBER OF ABNORMAL FINDINGS

	Cases
Cholangiogram normal	90 (64%)
Cholangiogram abnormal	50 (36%)
Total	140
Pancreatic duct shown	15 (11%)

It appears significant that a high percentage of abnormality in relation to the common duct may be expected in a consecutive series of operations on the biliary tract.

Demonstration of the main pancreatic duct (Fig. 4) is of little significance unless it, as well as the common bile-duct, is dilated, indicating a stenotic papilla.

TABLE II. ANALYSIS OF ABNORMALITIES IN 50 CASES

	Cases
(*a*) Stones in common bile-duct	27
(*b*) Abnormal dilatation	7
(*c*) Dilatation due to cancer of pancreas	6
(*d*) Dilatation due to pancreatitis	3
(*e*) Unexplained abnormality in common duct ..	3
(*f*) Common-duct stricture	2
(*g*) Accessory hepatic duct	1
(*h*) Aneurysm of hepatic artery..	1
Total	50

The 7 cases of 'abnormal dilatation' (*b*) included the 'false negatives' (described later) and cases of stenosis at the sphincter of Oddi.

'Unexplained abnormalities' (*e*) included filling defects, probably due to pancreatic nodules surrounding the common duct.

Two further common-duct strictures are included in (*a*), as there were stones above the stricture.

In (*g*) the cystic duct was seen to enter an accessory hepatic duct, which in turn joined the common hepatic duct. Without the help of the radiograph this duct may have been traumatized (Fig. 10).

TABLE III. FALSE INTERPRETATIONS RELATING TO STONES

False Negative Radiographs—3 *Cases* (0·85%).
1. Underexposed radiograph
2. Blurred radiograph (breathing movements)
3. Overfilled common duct

False Positive Radiographs—3 *Cases* (0·85%).
1. Gas-bubbles in common duct
2. Gas-bubbles in common duct.
3. Unexplained shadow in common duct

In the 'false negatives', radiographic technique was at fault in two instances. In the overfilled duct, no stones were shown on X-ray, but 8 stones were removed from the duct (Fig. 7).

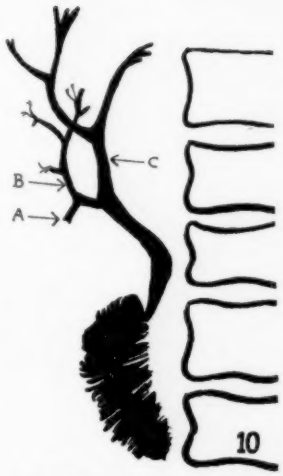

Fig. 10. Tracing of operative cholangiogram showing accessory hepatic duct at B. A indicates cystic-duct stump; C is the common hepatic duct.

In the 'false positives', gas-bubbles are the greatest sources of error; every care should be taken to eliminate this in the technique.

Faulty conclusions may also be made when the biliary tree is incompletely filled, when the dye does not flow into the duodenum because of temporary spasm of the sphincter of Oddi, or when the patient is wrongly positioned.

TABLE IV. RELATION OF JAUNDICE TO RADIOGRAPHIC FINDINGS

	Cases
No History of Jaundice: (84 cases)	
Common-duct stones found	8
Common duct clear	76
History or Presence of Jaundice: (54 cases)	
Common-duct stones found	19
Common duct clear	23
Other causes found	12
Doubtful History of Jaundice: (2 cases)	
Common-duct stones found	Nil
Common duct clear	2
Total	140

It will be noted that the absence of a history of jaundice does not exclude the possibility of stones in the common duct (Fig. 8). Also, though the patient may have had jaundice previously, stones are not necessarily present in the common duct at the time of operation.

TABLE V. OPERATIVE CHOLANGIOGRAMS—140 CASES

	Cases
Stones not felt in common duct, but shown on X-ray ..	8
Stones not shown on X-ray, but found in common duct	3

The fact that stones may be present in the common duct, yet not be palpable, especially by the inexperienced, demonstrates the value of an operative cholangiogram in such a case (Fig. 8).

DISCUSSION

A senior British surgeon has recently stated that operative cholangiography is 'only for the inexperienced and gadget-minded'. Frequently new procedures are accepted with reluctance by experienced men who have got on for many years without it. However, one would stress that operative cholangiography is a useful *additional* procedure to the well-recognized methods of searching for stones in the common duct.

It was inevitable that a biliary endoscope should be invented, and such an instrument has recently been described.

In many cases, stones will be discovered in the common bile-duct without help of X-rays. In a few cases stones not felt will be shown by X-rays, thus avoiding the mistake of leaving stones behind. It is alleged by some that forgotten stones will pass spontaneously; this probably only applies to very small stones.

Frequently a common duct packed with stones is encountered. How is one to be sure that every single stone has been removed? Control cholangiogram at the end of the operation is quite essential (Fig. 5).

Operative cholangiography can be of inestimable value in identifying anatomical stouctures. Often a duct is exposed in the gastro-hepatic omentum, and it may be impossible to identify it absolutely without the help of bouginage or contrast X-ray.

The discovery of an accessory hepatic duct on the X-ray will prevent damage to that structure (Fig. 10). Fig. 6 shows a case where the cystic duct ran a course parallel to the common duct right down to the ampulla of Vater!

Fig. 9 shows operative cholangiogram in a case of post-cholecystectomy biliary colic. There is a large cystic-duct stump, containing stones, and a common-duct stone.

A follow-up study on the present series of cases is necessary to establish further the value of operative cholangiography, and this will be undertaken in due course.

SUMMARY

1. The technique of operative cholangiography is described.
2. Possible dangers and complications are listed.
3. An analysis of 140 consecutive cases of operative cholangiography is presented.
4. We use operative cholangiography at every operation on the biliary tract, and can testify as follows:
(*a*) Very important information regarding pathology or abnormal anatomy in the biliary tree may be obtained.
(*b*) The team-work necessary is well organized at our general and private hospitals.
(*c*) Extra cost to the patient is small.
(*d*) There is no delay during the operation.
(*e*) Danger to the patient is negligible.
(*f*) It is essential that the procedure be performed accurately and with great care.

OPSOMMING

1. Die tegniek van operatiewe cholangiografie word beskryf.
2. Moontlike komplikasies en gevare word genoem.
3. 140 agtereenvolgende gevalle van operatiewe cholangiografie word hierbo ontleed.
4. Operatiewe cholangiografie is by ons 'n roetine by elke operasie op die galweë uitgevoer, en ons kan as volg rapporteer:
(*a*) Belangrike bevindings i.s. patologie of abnormale anatomie mag verkry word.
(*b*) Die spanwerk wat nodig is, is goed ge-organiseer by ons algemene en privaat hospitale.
(*c*) Koste verbonde aan die ondersoek, is gering.
(*d*) Die ondersoek verg min ekstra tyd gedurende operasie.
(*e*) Daar is min gevaar aan die ondersoek verbonde.
(*f*) Die ondersoek moet egter sorgvuldig en akkuraat uitgevoer word.

DIVERTICULA OF THE THORACIC OESOPHAGUS

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and

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Diverticula of the thoracic oesophagus are comparatively uncommon. Harrington[1] treated 216 patients with pharyngo-oesophageal diverticulum, while during the same period he treated only 8 patients with thoracic oesophageal diverticula. In an analysis of 1,600 patients admitted to the Out-patient Department of the Massachusetts General Hospital because of dysphagia, Macmillan[2] found less than 1% due to diverticula of the thoracic oesophagus. The true incidence of thoracic diverticula is probably much higher since these diverticula may produce no symptoms. Soulas,[3] states that from 1947 to 1951 the ratio of pharyngeal to thoracic pouches in his cases has been reversed, being now respectively 35 and 65%. The lower the level in the thoracic oesophagus, the greater the frequency of diverticula. In Vinson's review[4] of 42 cases of diverticula of the thoracic oesophagus, 24 were located in the lower third. The majority of cases occur in persons of the 40-60 age-group.

A pure topographical description such as middle third or lower third, epibronchial or epiphrenal pouches, is to be preferred to the terms traction pouches and pulsion pouches. These terms are probably misleading and inaccurate since a sum of primary and secondary factors is usually responsible (see below).

The pulsion type denotes protrusion of the wall or part of the wall which is produced by raising the intra-luminal pressure. The traction diverticulum results from fixation of a localized area of oesophageal wall to an adjacent structure more rigid than itself. With the contraction of scar tissue or the displacement of one structure away from the other, the oesophageal wall is dragged out in a tent-like fashion.

A pulsion-traction diverticulum means a combination of both types.

Barrett[5] gives a fascinating account of how chronic inflammation and calcification in the lymph system leads to shortening of strong bands of fibrous tissue between the anterior wall of the oesophagus and the epibronchial glands. These bands were originally described by Ribbert. Barrett also mentions that a few cases have been associated with adhesions in the vicinity of caries of the spine and pericarditis.

In view of the frequent occurrence of tuberculous adenitis, a tuberculous process can but rarely be a cause of epibronchial diverticula. Johnstone[6] believes that attachment of the oesophagus to the aorta results in the oesophagus being pulled away from the left bronchus as the aorta unfolds. If any adhesions exist between the oesophagus and the bronchus or its adjacent structures, traction diverticula may form, causing a potential weakness in the wall.

A primary factor in the aetiology of thoracic diverticula is an area of structural weakness created by gaps in the muscle wall of the oesophagus, associated with the passage of blood vessels.[7]

It is not difficult to visualize mucosa herniating through these weak spots in the oesophageal wall. Shaw,[8] in an excellent review of thoracic oesophageal diverticula, postulates that those pouches which do possess a muscle wall may equally well be explained as being complete congenital entities, subsequently enlarged. In support of this he cites those cases which have been reported post mortem and radiologically in the newborn infant and in older children.

Functional or false diverticula are simply areas of apparent pouching of the oesophageal wall, usually in the lower third, due to a local hypotonic state of the smooth muscle layer, associated with adjacent hypertonus or apparent stricture formation. They may often disappear at rest and are only thrown into prominence during what is usually abnormal peristalsis.

In addition to the primary factors such as areas of congenital weakness in the oesophageal wall and traction due to adherence of the oesophagus to surrounding structures, Shaw discusses the following secondary factors in his paper:

1. *Pulsion.* In the normal human oesophagus, primary and secondary peristaltic waves cause pressure sufficient to maintain a vertical column of water attached to its distal end at a height of 2½ feet. Several authorities regard this pulsion pressure as the most important single secondary factor in most cases.

2. *Anatomy of the lower oesophagus.* The majority of cases show pouching from the right lateral wall towards its anterior aspect, usually 2-3 inches above the diaphragm. In this situation the mechanical support of the peri-oesophageal tissues is least effective.

3. *Effect of cardiospasm.* This is not considered an important factor by Johnstone, who examined at least 200 cases of achalasia without finding a diverticulum. In a far greater number of cases of obstruction of the lower end of the oesophagus from other causes only one diverticulum was found. Shaw, on the other hand, quotes from 5 different papers in which cardiospasm has been an important contributing cause.

4. *Direct pressure of diverticulum.* The larger a dependent pouch becomes, the greater the tendency for its fundus to cause pressure on the subdiverticular oesophagus, thus setting up a vicious circle which may precipitate symptoms in a patient previously unaware of trouble.

5. *Atrophic changes.* With increasing age there is an inevitable small degree of atrophy in the muscular walls of the oesophagus, together with loss of elasticity in the supporting tissues and frequently some degree of chronic oesophagitis. These changes may partly account for the greater incidence in middle-aged and older people.

6. *Local sepsis.* Changes arising in the walls from chronic oesophagitis may also contribute to pouch formation. Adhesions due to extra-mural suppuration more often produce a primary effect by traction.

7. *Individual habits.* Certain bad habits, such as air swallowing, poor mastication and bolting of food, which are not uncommon in middle-aged edentulous men, have a well known association with oesophageal disorders.

Symptoms

Diverticula of the thoracic oesophagus sometimes produce no symptoms. The occurence of symptoms depends on the size of the diverticulum, the direction in which the diverticulum points, the size of the diverticular opening into the oesophagus, and associated conditions such as chronic subdiverticular stenosis or chronic oesophagitis. Small diverticula or diverticula which are directed upwards and have a wide opening into the oesophagus rarely produce symptoms. The actual symptoms may be chronic dyspepsia, retro-sternal discomfort and variable dysphagia. There may be intermissions due to varying degrees of oesophagitis. In rare cases the contents of a large pouch may be regurgitated on lying down.

Complications are those common to all diverticula of the gastro-intestinal tract, viz. infection, perforation, haemorrhage and malignant change.

Diagnosis

Radiology and oesophagoscopy are essential in diagnosis. The use of effervescent barium milk, which will rapidly find its way into a diverticulum and produce a clearly defined gas bubble with fluid level, is recommended. Shaw states that oesophagoscopy should be carried out with 4 principal objects in view:

1. To find the mouth of the pouch and evacuate its contents,

2. to examine the interior of the pouch and exclude the presence of malignant disease,

3. to take smears and biopsy material from any suspicious areas, and

4. to examine and explore the oesophagus in its whole length and to establish the presence and nature of any associated condition.

Treatment

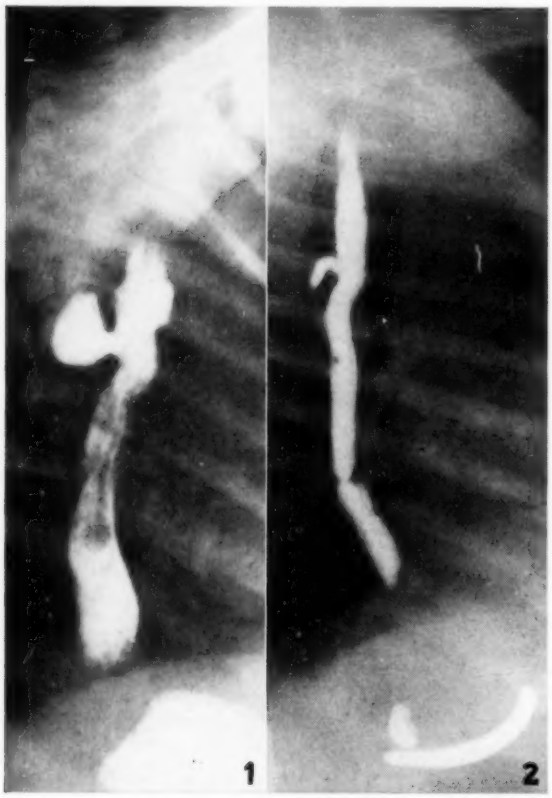
Pouches causing no symptoms require no treatment. In pouches associated with other pathological conditions the latter must be treated first. Surgical procedures employed are (1) extirpation of the sac, (2) diverticulopexy and (3) inversion of the sac. In cases of epiphrenic diverticula anastomosis between the diverticulum and the cardia of the stomach is sometimes practised.

CASE REPORT

C.A., aged 2½ years, a Coloured female child, was admitted to the Red Cross War Memorial Children's Hospital in October

1956 with the following history. She had been quite well until July of that year, when the mother noticed that she regurgitated food she had recently eaten. Since that time the child had subsisted on a milk diet, which was straining the family budget. There was no history of having swallowed corrosives or a foreign body.

On examination no clinical abnormality was detectable. The weight was 26 lb. and the Mantoux test (1 in 1,000 old tuberculin) was negative on two occasions.



A barium swallow (Fig. 1) was X-rayed, and an oesophageal diverticulum which projected backwards and slightly to the right was demonstrated. An area of narrowing was noted below the diverticulum.

On 22 October an oesophagoscopy (D.V.M.) was performed. The diverticulum was easily identified and a biopsy was taken from the thickened polypoidal mucosa around its opening. There was considerable narrowing of the oesophageal lumen immediately below the diverticulum, beyond which the only endoscope available on this occasion (a Negus child's oesophagoscope) could not be passed, so that the oesophagus distal to the diverticulum was not explored.

On histological examination of the biopsy specimen, the oesophageal mucosa was found to be infiltrated with chronic inflammatory cells. After the oesophagoscopy the patient was able to swallow without difficulty and she was accordingly discharged to be kept under out-patient observation. She did not, however, re-attend until 11 March 1957, when she was re-admitted, having experienced a recurrence of her former symptoms. The barium swallow was repeated and a similar radiological picture to that seen on her previous admission was obtained.

On 16 March the oesophagoscopy was repeated. Again with a Negus child's oesophagoscope the oesophagus below the diverticulum could not be entered. A child's bronchoscope was then used and with that a flat plastic foreign body, 20×8×2 mm., was identified below the level of the diverticulum and removed. The patient's subsequent course was uneventful and she was discharged on a normal diet.

On 10 June the barium swallow was repeated (Fig. 2) and this showed that the oesophageal diverticulum was considerably smaller than on the previous examination. The oesophageal lumen showed no abnormality.

The patient had remained free of symptoms.

Comment

This case is of interest because in the literature reviewed we have not seen a case of oesophageal foreign body associated with a diverticulum reported. It is suggested that oesophageal obstruction caused by the foreign body contributed to the periodic rise of intraluminal pressure, which resulted in a pulsion diverticulum.

The marked improvement in the patient's swallowing after the first oesophagoscopy was surprising. In retrospect a probable explanation for this was tilting of the foreign body into a less obstructing position as a result of the endoscopic manipulation.

Caffey[9] states that in children a foreign body should be carefully looked for whenever spasm and oesophageal obstruction are demonstrated.

When a barium swallow is carried out, a foreign body may cause one or more of the following abnormalities:[10]

1. A hold up of the column of barium. The object may be wholly or partly outlined by the barium and may be recognized by its shape.

2. A deviation or forking of the stream as the barium passes over the object.

3. A spasm or abnormal contraction of the oesophageal wall, usually at the point of impaction.

4. A small residue of barium, often like a streak, may remain stationary within the lumen. Attempts to dislodge it with drinks of water may at first be unsuccessful, because the barium adheres to a foreign body. On the other hand, fine streaks due to barium lying in mucosal folds are readily washed down. The outlining of the object with barium is the most valuable and characteristic sign.

The considerable reduction in size of the diverticulum in the present case after 3 months is interesting. We intend repeating the barium swallow examination in 6 months' time to ascertain whether the diverticulum has become smaller still.

SUMMARY

1. The incidence of thoracic diverticula is discussed.

2. A topographical classification of thoracic diverticula is recommended. The terms traction, pulsion and functional diverticula are defined.

3. The aetiology is discussed and brief mention is made of the symptomatology, diagnosis and treatment of thoracic diverticula.

4. A case of an epibronchial diverticulum associated with an oesophageal foreign body is reported.

We wish to express our sincere thanks to Prof. J. H. Louw for his helpful suggestions and criticism. We are indebted to Dr. A. B. Bull who administered the anaesthetics on both occasions and to Dr. E. van der Burg who was responsible for the X-ray investigations. We also wish to thank Dr. H. Reeve Katzeff,

Acting Medical Superintendent, Red Cross Children's War Memorial Hospital, for permission to report this case.

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CASE OF ALBERS-SCHÖNBERG'S DISEASE REVIEWED AFTER 20 YEARS

JULIUS H. KRETZMAR, M.B., CH.B. (EDIN.)

and

JEAN TIDBURY, M.B., CH.B., D.M.R.

Kimberley

In 1936 a case of Albers-Schönberg's disease[1] was described by one of us (J.H.K.) and R. A. Roberts,[2] with photograph and X-ray plates. In January 1956, about 20 years later, the patient presented herself again and the skeletal system could again by X-rayed to assess the present state of her bones.

In the intervening years she had suffered no serious illnesses, had had one infant, and was now wearing glasses and using a hearing aid. Her only complaint now was a neuralgic pain in the right half of the face. She had had some teeth extracted without any ill effect to the mandible. In all the years she had never had any fracture of any of her bones.

Fig. 1. (Published in Brit. Med. J., 25 April 1936, **1**, 837.) The patient in 1936, when 21 years old. Note the wide separation of the eyes, indicating some degree of ocular hypertelorism, the prominence of the nasal bone, the left-sided facial paralysis, and the massive lower jaw.
Fig. 2. The patient in 1956, for comparison. Note the great massiveness of the lower jaw.

Clinically no untoward pathological departure from the normal could be detected other than features seen in 1936 and still readily visible on inspection—exophthalmos, facial paralysis and the massive lower jaw (Figs. 1 and 2). The great increase in bulk of the lower jaw was particularly striking, the heavy broad bone being palpated only by a wide separation of the fingers. X-ray films reveal the gross appearance.

As in 1935, X-raying of the skull called for a heavy exposure before satisfactory films could be procured, and the features are very much the same as reported then. The rest of the skeletal system, thoracic cage, humerus, hands, spine, pelvis, femur and feet were all X-rayed again and also reveal no appreciable changes from the skiagrams described in 1936, other than those associated with growth. No evidence of fractures was detected. There was no appreciable additional narrowing of the medullary cavities of the long bones. The only really striking change from the appearance of 20 years ago, was the heavy massiveness of the broad lower jaw, while the X-ray films of the skull once again reveal the thickening of the occipital region and the homogeneous thickening of the whole base of the skull. Biochemical examination of blood and urine revealed nothing abnormal.

In 1937 Falconer[3] reported a case of generalized osteosclerosis of familial type, with facial and other deformities. The patient (male) was sent into hospital from Ladismith, Cape, by Blyth, and his sister was reported as suffering from even greater facial deformitity due to marked thickening of the upper and lower jaws. Falconer compared his case with our present case (as reported in 1936[2]) and stated: 'There can be no doubt that Kretzmar and Roberts' case and the present case are identical. Neither Dr. Roberts nor Dr. Blyth are able to trace any relationship between the two families, but as they both come from the Cape Province, it is not altogether excluded'.

Further questioning of the patient in 1956 on this same point elicited the fact that she knew of no branches of the family tree in the neighbourhood of Ladismith, Cape.

'The present case', Falconer stated in conclusion, 'Dzierzynsky's first family, and Lauterburg's case,[4-5] all have in common a generalized osteosclerosis affecting several members of the family with involvement of both the base and

vertex of the skull, the bones of the face and a characteristic alteration of the shape of the metacarpals. There is no tendency to increased fragility of the bones. There are no associated blood changes and the condition apparently runs a benign course. They would appear to present a definite entity. Although there is no evidence of family involvement in Kretzmar and Roberts' case the clinical and radiological features are so absolutely identical that it also must be included in this group'.

From a recent extensive review of the literature on 'osteopetrosis in adults' by Hinkel and Beiler[6] it would appear that the case reported by us falls in the category of the benign type of Albers-Schönberg's disease, where the patient may continue enjoying good health, without suffering from anaemia and without the repeated occurrence of pathological fractures.

SUMMARY

A case of Albers-Schönberg's disease examined in 1935 and reported in 1936 is reviewed in January 1956. No significant changes are revealed in the X-ray films of the skeletal system compared with the descriptions of 20 years ago. There is no history of any fracture in the 20 years and the general health of the patient has been good.

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ALGEMENE WENKE OOR X-STRAALONDERSOEKE

C. J. B. MULLER, M.B., CH.B., D.M.R.

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Die meeste pasiënte het geen benul van wat hulle moet doen of verwag wanneer hulle vir 'n X-straalondersoek verwys word nie. Hier volg kortliks my persoonlike opinie omtrent die inligting:

Kleding. Warm katoen of wol onderklere, sonder knope, word verkies. 'n Kamerjas en pantoffels kom ook handig in.

Barium-kliesma. In gevalle van hardlywigheid word cascara twee aande voor die ondersoek aanbeveel. Die aand voor die ondersoek moet die pasiënt 'n deeglike uitspoeling kry, asook 'n tweede uitspoeling 'n uur voor die ondersoek. Hiervoor word gewone saline gebruik; eers 3 pinte wat dan uitgelaat word en dan een of twee maal herhaal word totdat die ontlasting geen faeces meer bevat nie. Die ondersoek duur omstreeks 'n uur. In geval van ouerige persone is dit altyd raadsaam om 'n ekstra stel onderklere saam te bring.

Barium-maal. Vanaf die vorige aand moet die pasiënt mondeliks niks neem nie. 'n Slukderm-, maag- en duodenum-ondersoek duur gewoonlik 'n uur. Indien die hele spysverteringskanaal ondersoek word, strek dit tot 24 uur.

Appendiks-maal. Die barium word die vorige aand gedrink en die appendiks wys die volgende oggend. Indien die appendiks nie met barium gevul is nie, word plate weer die middag geneem en moontlik die volgende oggend herhaal. Hierdie ondersoek kan dus 3 dae duur. Nog 'n plaat word 72 uur nadat die appendiks gevul het, geneem om vas te stel of daar stasis is.

Swangerskap. Dit is onwenslik om die fetus aan enige bestraling bloot te stel en tensy daar 'n dringende nediese rede is, behoort geen buikondersoek ooit gedoen te word nie.

Galblaas-ondersoek. 'n Volledige, vetterige middagmaal moet die dag voor die ondersoek geëet word sodat die galblaas goed kan krimp. 'n Ligte, vetvrye, aandete word dan genuttig en omtrent 9 nm. moet die kleurstof pille een na die ander met water geneem word. Hierna moet niks per mond geneem word totdat die ondersoek die volgende oggend gedoen is nie. Hierdie eerste deel duur omstreeks 1 uur waarna die pasiënt dan 'n vetterige maal moet nuttig; 2 tot 3 uur later word nog 'n plaat geneem. Die hele proses duur omtrent 5 uur. Vir die binneaarse biligrafin ondersoek is die voorbereiding dieselfde maar die pasiënt neem geen pille nie.

Binneaarse Piëlogram. Kasterolie of cascara word die vorige dag geneem. Geen vloeistof mag 15 uur lank vóór die ondersoek geneem word nie. Ook hier word 'n uitspoeling 1 uur voor die ondersoek aanbeveel, indien die pasiënt hardlywig is. Die ondersoek self duur omtrent 1-2 uur.

Salpingogram. Die ondersoek word gewoonlik 1 week ná die maandstonde gedoen. Die voorbereiding is dieselfde soos vir 'n buikondersoek. Dit duur omtrent 'n uur.

Bronchogram. Waar bronchiectase vermoed word, moet posturale dreinering vir 24 uur voor die bestelling baie deeglik toegepas word. 'n Toets vir allergie teenoor cocaine moet ook vooraf gedoen word. Toediening van 'n kalmeermiddel een uur voor die ondersoek is wenslik. Die ondersoek self duur 1½ uur.

Akute Buikondersoek. Hier word staande, liggende en laterale opnames geneem. Die duurte van die ondersoek is 'n halfuur. Daar is geen voorbereiding vir skedel, werwelkolom, gewrigte, bekken, borskas, hart of longe vereis nie, en dit duur ½-1 uur.

Kinders. 'n Kalmeermiddel soos Seconal, chloral hydrate ens., 'n uur voor 'n ondersoek help baie.

Miëlogram, encephalogram en *ventriculogram-ondersoeke* word verkieslik in 'n hospitaal se X-straal-afdeling gedoen en duur ongeveer 1-2 uur.

Koste van ondersoek. Die meeste pasiënte sal verkies om 'n idee van die koste van ondersoeke te hê alvorens hulle verwys word. Hier volg kortliks die gewone vasgestelde fooie in die stede van Suid-Afrika waar die ondersoek deur 'n radioloog gedoen word:

	£	s.	d.
Gewrigte	3	3	0
Werwelkolom (1 deel)	5	5	0
Hele ruggraat	12	12	0
Longe	4	4	0
Hart	5	5	0
Galblaas	6	6	0
Barium-maal (maag en duodenum), binneaarse biligrafin, galblaas, binneaarse piëlogram, bariumkliesma, salpingogram, bronchogram	8	8	0
Volledige Barium-maal	12	12	0

Waar die ondersoek besonder moeilik is en lank duur, kan die fooie met een-derde vermeerder word.

Uitslae is gewoonlik 24 uur nadat die ondersoek voltooi is beskikbaar.

In gevalle waar die pasiënt van ver kom en daar twyfel bestaan of die pasiënt aan galblaas of maag-patologie ly, kan 'n cholecystogram en barium-maal op dieselfde dag gedoen word mits die pasiënt die kleurstofpille die vorige aand geneem het.

Verwysing van pasiënte na opleidingshospitale vir X-straalondersoeke. Dit is 'n voorwaarde dat X-straalondersoeke nie uitgevoer mag word tensy die pasiënt die gewone privaat-fooie nie kan bekostig nie en deur die Buite-Pasiënte-afdeling se medici verwys is nie. Onder spesiale omstandighede mag privaat-pasiënte gedoen word.

Die gevaar van oortollige bestraling as gevolg van X-straalonder-

soeke. Dit word al hoe meer beklemtoon dat die X-straaleenheid 'n gevaarlike bron van bestraling is. Die klein draagbare eenheid is 'n nuttige en veilige apparaat waar die gebruik daarvan beperk word tot gewrigte- en borskas-ondersoeke. Wanneer dit vir deurligting gebruik word deur iemand wat nie vir radiologiese werk opgelei is nie, kan dit gevaarlik wees omdat dit op 'n 18 duim buis-pasiënt-afstand 'n dosis van 10r per minuut kan lewer en 'n paar minute deurligting kan dan oortollige bestraling veroorsaak.

Algemene diagnostiese ondersoeke skep geen gevaar vir die pasiënt nie, maar by alle persone onder 40 jaar is dit wenslik om die geslagsorgane sover moontlik te beskerm, aangesien oortollige bestraling daarop moontlik genetiese gevolge mag hê. Dit is veral van belang by babas en klein kinders. Die X-straalondersoek van enige deel van die liggaam lewer 'n sekere dosis bestraling op die geslagsorgane deur spatting van die strale. Die persoon wat die ondersoek doen is ook aan die strale blootgestel.

MEDICAL DIRECTORY

The Southern Transvaal Branch Council of the Medical Association has directed an enquiry to the South African Medical and Dental Council on the subject of the circular issued by Messrs. Knox Printing Company inviting medical practitioners to supply information concerning themselves for publication in a medical directory. Dr. J. Gluckman, Hon. Secretary of the Branch, has received the following reply, dated 13 September 1957, from the Registrar of the Medical Council:

'I beg to acknowledge the receipt of your letter of the 9th instant, in regard to a circular sent out by Messrs. Knox Printing Company.

'Some little while ago the Council received enquiries from the publishers of other directories enquiring whether the names of medical practitioners and dentists may be included therein. The Council advised the enquirers that medical practitioners and dentists are entitled to furnish them with such general information concerning their careers as would be required for publication, provided that the material was not presented in such a manner as to cause the individual to contravene the Council's rules and more especially those rules relating to advertising.'

NEW PREPARATIONS AND APPLIANCES : NUWE PREPARATE EN TOESTELLE

Amargyl

Maybaker (S.A.) (Pty.) Ltd. announce the introduction of 'Amargyl' brand chlorpromazine/amylobarbitone tablets each containing 25 mg. of chlorpromazine hydrochloride and 50 mg. of amylobarbitone, and supply the following information:

This association of drugs brings about considerable alleviation or even symptomatic cure in various states of anxiety and depression, and at the same time renders patients more amenable to psychotherapy. The potentiating effect of chlorpromazine on barbiturate action allows the amylobarbitone to be used to full clinical effect in considerably reduced dosage.

'Amargyl' is presented as lime-coloured sugar-coated tablets in containers of 50 and 500.

* * *

Natabec Kapseals

Parke, Davis Laboratories (Pty.) Ltd. announce the introduction of Natabec Kapseals, a new vitamin-mineral supplement for pregnant and lactating women, and supply the following information:

The aim of good obstetric care, from early pregnancy through lactation, is to provide better health for the mother and child. Nutritional essentials are not always included in the daily diet and Natabec contains vitamins and minerals carefully selected to meet the requirements of pregnancy and lactation.

In contradistinction to many other vitamin-mineral supplements an outstanding feature of Natabec is the inclusion of calcium carbonate in preference to one of the calcium phosphates. Drs. Page and Page in *Obstetrics and Gynecology* (1953): **1**, 94, reported that muscle cramps often occur in obstetric patients and attributed this to a high level of phosphorus in the diet. These can be either prevented or relieved to a significant degree by reducing the amount of phosphorus in the diet and by the use of calcium salts free of phosphorus.

Indications: Natabec is indicated as a vitamin-mineral dietary supplement during pregnancy and lactation.

Dosage and Administration: One or more Kapseals daily. Each Kapseal of Natabec contains:

Calcium carbonate	600 mg.
Ferrous sulphate	150 mg.
Vitamin B_{12} (crystalline)	2 mcg.
Intrinsic factor concentrate	5 mg.
Folic acid	1 mg.
Synkamin (vitamin K5)	0·5 mg.
Rutin	10 mg.
Vitamin A	4,000 units
Vitamin D	400 units
Vitamin B_1 mononitrate	3 mg.
Vitamin B_2 (riboflavin)	2 mg.
Vitamin B_6 (pyridoxine hydrochloride)	1 mg.
Nicotinamide	10 mg.
Vitamin C (ascorbic acid)	50 mg.

Package Information: Bottles of 25 Kapseals.

PASSING EVENTS : IN DIE VERBYGAAN

World Congress of Anaesthesia. It has been announced that the Second World Congress of Anaesthesia will be held in Toronto, Canada, during August or September 1960.

* * *

Workmen's Rehabilitation Centre. The next clinical meeting of this Centre, corner of Esselen and King George Streets, Hospital Hill, Johannesburg, will be held on Tuesday, 29 October, at 5.15 p.m., in the Gymnasium. Mr. C. W. Law, F.R.C.S. will speak on 'Contracture of Hand,' and Mr. D. H. Walker, F.R.C.S. on 'Early and late skin replacements after injury'. All doctors are cordially invited to attend and join in ensuing discussions.

* * *

Maybaker (S.A.) (Pty.) Ltd. announce that their Port Elizabeth warehouse and factory and Johannesburg depot will be closed from 16 December 1957 to 5 January 1958. To avoid the holiday period orders should be placed earlier. During the holiday period the usual supplies can be obtained from wholesalers. Urgent orders will be executed by an emergency service at Port Elizabeth.

* * *

Dr. Selig Sacks, M.B., Ch.B. (Cape Town), D.O.M.S. (R.C.P. & S.) has joined Dr. A. W. S. Sichel in practice as a Specialist Ophthalmologist at National Mutual Building, 17 Church Square, Cape Town. Telephones: rooms 2-1629, Dr. Sichel's residence 7-2996, Dr. Sacks' residence 6-6606. Dr. Sacks has been working in London as an ophthalmologist for the past 10 years, and has held posts as ophthalmic registrar at St. Thomas's Hospital and senior registrar at the Western Ophthalmic Hospital (St. Mary's Hospital).

* * *

Dr. A. J. Wrigley, of St. Thomas's Hospital, London, and Mrs. Wrigley sailed for England from Cape Town in the *City of Port*

Elizabeth on 16 October. Dr. Wrigley had been spending some weeks in South Africa, having attended the South African Medical Congress, Durban, in September at the invitation of the Medical Association of South Africa. He delivered addresses in various parts of the Union, as well as at the Congress and, as official observer, attended the examinations recently held in Cape Town by the South African College of Physicians and Surgeons in Obstetrics and Gynaecology. Dr. and Mrs. Wrigley were bidden farewell on the ship by Dr. D. P. de Villiers and by Dr. J. C. Coetzee, with whom they had been staying for a few days. Dr. and Mrs. Wrigley have much endeared themselves to the South African friends in different parts of the country with whom they have stayed or otherwise come in contact. Dr. Wrigley spoke appreciatively of the kindness and hospitality he had received and of the opportunity he had been given of obtaining an intimate insight of professional and other sides of life in South Africa.

* * *

Union of South Africa. Department of Health. Notification of formidable epidemic disease and poliomyelitis in the Union during the period 4 October-10 October 1957.

Poliomyelitis

	Eur.	*Nat.*	*Col.*	*As.*	*Total*
Transvaal	1	–	–	–	1
Cape Province ..	1	–	–	–	1
Orange Free State..	–	–	–	–	–
Natal	2	–	–	–	2
Totals ..	4	–	–	–	4

Plague. Cape Province: The Kibikwe Reserve, portion of Morokweng, district Vryburg, can now be regarded as free from infection as no further cases have been reported since the notifications in Newsletter No. 37 of 1957.

Small pox,Typhus Fever: Nil.

* * *

The Vth International Congress on Diseases of the Chest, sponsored by the International Affairs Council of the American College of Chest Physicians will be held in Tokyo, Japan, on 7-11 September 1958. The Japanese Government is issuing invitations to the Governments of all countries with which it has diplomatic relations for the appointment of delegates to the Congress. It is thus hoped that delegations from every country in the world will be present for the Congress in Tokyo. The American College of Chest Physicians has 5,935 members in 86 countries and territories and it is expected that each of these countries will be represented by delegates at this Congress. Requests for places on the scientific programme will be considered by a special committee of the College, and authors of papers which can be accepted will be notified promptly so that they may commence work on the preparation of their manuscripts. All abstracts must be received before 1 January 1958. Scientific papers, panel discussions and 'fireside conferences' will be presented on the following subjects: Coronary disease; Occupational diseases of the chest; Benign and malignant chest tumours; Tuberculosis; Cardiopulmonary function studies; Asthma and emphysema; Cardiovascular surgery; Broncho-oesophagology; Tropical diseases of the chest; Aetiology of lung cancer; Paediatric cardiology; Metabolic disorders; Miscellaneous topics on chest diseases.

The Official Travel Agents for South Africa are Springbok Safaris Pty. Ltd., 29 Leyds Street, Johannesburg.

Further information can be supplied by the Regent of the College for South Africa, Dr. D. P. Marais, Southern Life Building, St. George's Street, Cape Town and by the Governors, Dr. T. Schrire, P.O. Box 643, Cape Town and Dr. M. A. Pringle, Springkell Sanatorium, North Rand, Transvaal.

REVIEWS OF BOOKS : BOEKRESENSIES

RUDOLF STEINER EDUCATION

Rudolf Steiner Education. A brief exposition. By L. Francis Edmunds. Pp. 65. 3s. 6d. Sussex: New Knowledge Books. 1956.

Contents: Foreword—by the Editor, "Child and Man". *Introduction.* The Kindergarten and Pre-School Years. The Years with the Class Teacher. Adolescence. Questions—general and particular. The Form and Organization of a Rudolf Steiner School. The Range of Rudolf Steiner's Work for Children. The Rudolf Steiner School Movement.

Man, according to the recapitulation theory accepted by the anthroposophicals, re-lives the history (ages) of human society ('each human life is the revelation of an immortal spirit that was before birth and that will be after death'). The aim of Steiner's anthroposophical education is to help the child to move and live in intimate harmony with this 'spirit'.

The child passes through 3 clearly marked phases in its growth. During the first 6 or 7 years of human life, all forces are directed towards building up the *physical* organism. In the Nursery and Transition classes therefore, as was the spirit in primitive society, the stress is on activity, the children learning through imitation and example. With the *change of teeth* a certain stage of completion is reached, and this is accompanied by a definite change in mental outlook.

From 7 to 14—a period only given to man—children live in the world of their *feelings* and in this realm *art* makes a direct appeal and all subjects, even mathematics are presented in an artistic and symbolic way. During these critical years each class is entrusted to a class teacher who remains with it for the whole 8 years, teaching all the main subjects etc.

After 14 the *intellect* is ready to function, because children now experience the world through the power of thought and have a natural desire to submit everything to reason. Periods in these co-educational schools are blocked and subjects are taught in block periods of some 4 weeks each. (Co-education does not necessarily mean boys and girls educated together, but science and art being rightly related.).

It is also claimed that many non-normal or handicapped children have received great benefit from this system, partly because they are looked upon as presenting a constant moral challenge to modern society.

Mr. Edmunds' book could have given the layman more information on organization and administration. On the other hand, it serves as a good introduction to the Steiner system, and a challenge for teachers, parents, mental-health specialists, and those who are looking for some new philosophy of education. For those, however, with a convinced religious philosophy, the information would have to be presented much more inspiringly.

S.P.O.

ELEMENTARY ANATOMY AND PHYSIOLOGY

Whillis's Elementary Anatomy and Physiology: Fourth Edition. By Roger Warwick, B.Sc., Ph.D., M.D. Pp. vii + 274. With 107 Illustrations. London: J. & A. Churchill, Limited. 1957.

Contents: I. The Human Body. II. Osteology. III. The Joints or Articulations. IV. Muscles and Fasciae. V. The Alimentary System. VI. Digestion. VII. The Blood. VIII. The Circulatory System. IX. The Principal Blood-Vessels of the Body. X. The Lymphatic System. XI. The Respiratory System. XII. The Fate of Absorbed Foodstuffs, Metabolism. XIII. The Urinary System. XIV. The Nervous System. XV. The Special Senses. XVI. The Genital System. XVII. The Skin. XVIII. The Ductless Glands. XIX. The Spleen and the Liver. Appendix on Nomenclature. Index.

This book was written so as to link elementary human anatomy with some simple physiology for the first-year medical student, and it will also be of value to trainee nurses, physiotherapists and radiographers.

Although Professor Warwick claims in his preface that this 4th edition has been brought up to date from the point of view of recent contributions in anatomy and physiology and of terminology, there are still a number of antiquated descriptions and terms included. The most glaring example is the text dealing with the structure of the lung and Fig. 80 which illustrates it. Only

3 components (and these excluding B 12) of the vitamin-B complex are mentioned. A further example is the method indicated for compression of the axillary artery (p. 136), viz., placing a pad in the armpit and bringing the arm closely to the side, which can only result in a bloody disaster.

In general the illustrations are large and clear but rather 'flat'. The chapters dealing with the locomotor apparatus are good. This book is recommended as a reference book to the above-mentioned trainees. It may also be of use to a good medical student who wishes to do a rapid revision of basic elementary anatomy and physiology just before entering his clinical years.

R.S.

STATISTICS

Mathematics and Statistics for Use in Pharmacy, Biology and Chemistry. By L. Saunders and R. Fleming. Pp. x + 257. 27s. 6d. (postage 1s.). London: The Pharmaceutical Press. 1957.

Contents: Introduction. Preface. 1. Arithmetic. 2. Algebra. 3. Graphs. 4. Series, e and natural logathms. 5. Differential calculus. 6. Higher derivatives and partial differentiation. 7. Integration. 8. Trigonometry. 9. Differential equations. 10. Equations and series for describing experimental measurements. 11. Probability. 12. Statistical analysis of repeated measurements. 13. Comparison of data by statistical methods. Tests of significance. 14. Some applications of statistics to biological assay and bacteriology. 15. Some applications of statistics in pharmacy. *Appendix I.* Fundamental constants, approximations and conversion factors. *Appendix II.* Triangles, lengths, areas, volumes and analytical geometry. *Appendix III.* Standard integrals. *Appendix IV.* Stirling's approximation. *Appendix V.* Mean and variance of the binomial and Poison distributions. *Appendix VI.* The normal distribution. *Appendix VII.* Variance of a function of variates. *Appendix VIII.* Some theorems in statistics. *Appendix IX.* Regression variance. *Appendix X.* Determinants. *Appendix XI.* Solution of the diffusion equation. *Appendix XII.* Binomial theorem for any index. *Appendix XIII.* Statistical tables. Four-figure Logarithms. Four-figure Antilogarithms. Answers to Problems. Index.

This is a text-book written for the reader who feels a positive need for a knowledge of mathematical theory and its application to biology. It is by no means light entertainment for the occasional consumer of popular science. The author presumes no previous knowledge of the subject, but they do expect concentration, a modicum of common sense and a measure of diligent application. For those who fall within the circle of readers intended by the authors the reading of this work will be well rewarded effort.

The book starts with a definition of the 'alphabet' of arithmetic and in the first 100 pages deals minutely with the theory of algebra, logarithmic mathematics, trigonometry, differential calculus, and the solution of partial differential equations. The authors could not have covered so vast a territory without loss of detail, sequence or clarity had they not abandoned the literary style of 'easy narrative'. The fact that they have done so adds immeasurably to the value of the book and makes their introductory apology unnecessary.

It is doubtful if the section on statistics will replace other standard works on the subject or consultation with the professional statistician. It will, however, place either course of action on a sound theoretical basis and facilitate the evaluation of published results which embody statistical argument.

This is a work to be heartily recommended as an advertisement for British academic pharmacy and biology.

E.B.D.

A TEXTBOOK OF PHYSIOLOGY

The Life of Mammals. By J. Z. Young, M.A., F.R.S. Pp. vii + 820. Illustrations. 84s. Oxford: Oxford University Press. 1957.

Contents: Section I. The Control of Living Systems. *Section II.* The Skin, Control of Temperature and Appearance. *Section III.* The Connective Tissues. *Section IV.* Skeletal Tissue, Cartilage and Bone. *Section V.* The Framework of the Body. *Section VI.* Muscles. *Section VII.* The Vertebral Column. *Section VIII.* The Forelimb. *Section IX.* The Pelvic Girdle and Hind Limb. *Section X.* The Head of Mammals. *Section XI.* The Intake of Food, Mouth and Teeth. *Section XII.* Digestion. *Section XIII.* The Internal Environment and Composition of the Body Fluids. *Section XIV.* The Heart and Circulation. *Section XV.* Respiration. *Section XVI.* Excretion and the Control of Water Balance. *Section XVII.* The Nervous System. *Section XVIII.* The Spinal Cord. *Section XIX.* The Organization of the Brain. *Section XX.* The Autonomic Nervous System. *Section XXI.* The Control of Posture and Movement. The Cerebellum and Midbrain. *Section XXII.* The Forebrain. *Section XXIII.* The Cerebral Cortex. *Section XXIV.* Receptor Organs. *Section XXV.* Receptors in the Skin and Viscera. *Section XXVI.* The Eye. *Section XXVII.* Receptors for Space Orientation and Air-borne Vibrations. *Section XXVIII.* Chemoreceptors. *Section XXIX.* Endocrine Organs. The Thyroid, Parathyroid and Thymus. *Section XXX.* The Adrenal Glands. *Section XXXI.* The Pituitary Gland. *Section XXXII.* The Pancreatic Islets and the Control of Carbohydrate Metabolism. *Section XXXIII.* Internal Secretions and Homeostasis. *Section XXXIV.* The Course of Development. *Section XXXV.* The Ovum and its Fertilization. *Section XXXVI.* The Production of an Embryo, Cleavage and Gastrulation. *Section XXXVII.* The Sequence of Differentiation. *Section XXXVIII.* A Comparative Survey of Gastrulation in Vertebrates. *Section XXXIX.* Extra-Embryonic Membranes. *Section XL.* The Reproductive Tract of Mammals. *Section XLI.* The Oestrous Cycle of Mammals. *Section XLII.* The Development of Mammals. *Section XLIII.* Segmentation, Development of Skeleton, Muscles and Coelom. *Section XLIV.* Development of the Gut and Respiratory System. *Section XLV.* Development of the Urogenital System. *Section XLVI.* Development of the Blood Vascular System. *Section XLVII.* Development of the Nervous System. Bibliography. Index.

This magnificent work by the eminent anatomist and physiologist, Professor J. Z. Young, F.R.S., is a publication of the first importance.

The book astonishes one by the breadth of its scope. It embraces literally the whole of mammalian physiology, and may be considered the author's *magnum opus*. No mammal too insignificant for Professor Young's analyzing eye, and none too large. From the development of the mouse to a description of the tail of a whale, all are brought under one great review in this general perspective of mammalian physiology.

This is a book for study and for reference. All sorts of facts are mentioned; the ovulation of the spiny ant-eater is considered as well as the blastocyst of the badger, and the broad and solid basis of general mammalian physiology makes this the 'Starling' of the mid-century. The very full chapters on development and embryology are of particular interest and value.

Through the whole of the book there runs the theme of the relationship between structure and function. It is the standard text-book on physiology, which we recommend to students of biology, to medical students and to physiological workers. The format is good, the line drawings are clear and concise and the index adequate. It is an interesting coincidence that Starling, of University College, London, whose 'Elements of Human Physiology' guided thought and research in the early part of the century, should be succeeded by an author from the same medical school 50 years later, this time from its Department of Anatomy.

The author, University College, and the publishers are to be congratulated on bringing out a great book.

S.T.

THE PLEA FOR THE SILENT

The Plea for the Silent. With an Introduction by Dr. Donald McI. Johnson, M.P. and Norman Dodds, M.P. Pp. 176. 12s. 6d. net. London: Christopher Johnson Publishers Ltd. 1957.

Contents: Introduction by *Dr. Donald McI. Johnson, M.P. and Norman Dodds, M.P.* No Benefit of Jury. An Unnecessary Stigma. A Broken Window. Strange Therapeutics. Into the Unknown. Fear Gripped Me. A Doctor's Story. The Country of the Insane. Legality Against Justice, *as told by E. Pakenham-Walsh, I.C.S. (retd.).* Epilogue, *by* Leonard W. Clark, M.A. (Oxon.), F.R.A.S.

This interesting book is made up of the stories of persons who have had personal experience of the somewhat antiquated laws of England in regard to mental disease. They give only one side of the picture and one must not forget that there is another side. The conditions described certainly merit attention and improvement, and one would wish the compilers of the book all success in their campaign to have more enlightened methods and sur) roundings introduced as a change from the rather mediaeval conditions which are described.

A.H.T.

FLUID BALANCE IN SURGICAL PRACTICE

Fluid Balance in Surgical Practice. 2nd Edition. By L. P. Le Quesne. 20s. net. Pp. vii + 140. London: Lloyd-Luke (Medical Books) Limited. 1957.

Contents: Preface. Physiological Considerations. Effects of Operation on Water and Electrolyte Balance. Administration of Fluid and Electrolytes in the Uncomplicated Case. Dehydration. Potassium Deficiency. Renal Failure: Anuria. Effects of Excess Water and Salt. Nitrogen and Calorie Problems. Fluid Balance in Children (by Brian W. Webb). Technical Considerations. References. Appendices Index.

The first edition of this monograph appeared in 1954 and was based on the Moynihan Prize Essay for 1953. This always results

in an unsatisfactory method of presentation as the book is then written to satisfy the conditions of the essay rather than to present the subject as a whole.

Now, however, comes the second edition which has not only been brought up to date but the disproportion between its various sections, resulting from the conditions of the original prize essay, has been corrected. To achieve this there has been extensive revision and some additions have been made. Thus nitrogen and calorie problems receive more detailed consideration and a completely new section is included on the problems of fluid balance in infants and children undergoing surgery. This latter section has been written by B. W. Webb, Senior Registrar, Children's Department, King's College Hospital.

All this improvement has resulted in an excellent little book which should be read from cover to cover by all surgeons and others who are faced with these problems. The text is clear and easy to understand and it presents the whole subject in a readily assimilable form; the recommendations are completely practicable and safe. The only justifiable criticism one can offer is that the problem of the alkalosis which occurs with potassium deficiency is presented in a rather confusing manner, probably for the sake of brevity; some expansion here may help to clarify what is admittedly a confusing problem.

But that is a minor point. Here is a monograph which must be recommended very strongly and much trouble and many lives will be saved if all house-surgeons read this book before entering the surgical wards.

D.J. du P.

CORRESPONDENCE : BRIEWERUBRIEK

MEDICAL AID FEES

To the Editor: The following I feel will be of real interest to every medical practitioner. It is the question of taking pathological specimens for members of medical aid societies and also delivering them to the laboratory, which often involves a trip of 3-4 miles, even in a smaller town. Are we expected to take the blood and also deliver the specimen to the laboratory for the fee of a single consultation?

I refer to a concrete case: I was consulted, found it necessary to take blood, did so at the time of the first consultation, and delivered it to the laboratory, which of course meant transport and time. Can I charge only for a single consultation? This important factor was apparently overlooked in the new tariff.

I also want to learn what the position is with pathological examinations done by many of us at our rooms, e.g. blood sedimentation test? Are we expected to include it in the ordinary consultation fee laid down?

The question of the 'first' consultation must receive attention. Surely it is not unreasonable to suggest that for a 'first' consultation, which should take at least 30-40 minutes, the fee should be increased, just as for a specialist? The medical aid societies must see the justification for this suggestion, even if they suggest that the member is to pay the difference. It is high time that we senior practitioners, with years of experience, should demand a higher fee. Even the Government offers higher salaries to men with experience, in contrast to recently qualified and inexperienced practitioners. This seems logical enough.

In conclusion: Is any practitioner, because he is a member of the Medical Association, committed to accept people for treatment because they are members of a medical aid society, for the fees agreed upon, or has he the right to inform the patient that the difference of the fee charged must be his responsibility? We are frequently consulted by members of the S.A.R. & H. and other similar medical funds, who are prepared to pay the full fee! Why?

A Member since 1927

The Associate Secretary of the Medical Association writes: The question of the delivery of specimens to a pathological laboratory has not previously been raised. In all probability practitioners have delivered specimens as a courtesy to their patients or have found a member of the patient's household prepared to do so for them.

Practitioners should not charge additional fees for such routine tests as are carried out in order to arrive at a diagnosis, but fees may be charged for certain additional pathological tests, of which blood sedimentation rate is one. These tests are specified in the section for general practitioners on page 4 of the tariff book.

The first consultation of a specialist is remunerated at a much higher fee than subsequent consultations, because of the detailed nature of the examination. The fees for a general practitioner are the same right through and the short consultations are supposed to make up for the additional time taken in long consultations. The fee for the senior practitioner is a different question altogether.

A medical practitioner is not bound to accept any patient at medical aid rates, but must inform the patient accordingly *at the first consultation or visit*. The patient will then be personally responsible to the doctor for the whole account. If the doctor accepts the patient as a member of the medical aid society, he may only charge the agreed tariff rate and, if the society pays the amount, he must accept that payment *in full settlement* (see page 1, paragraph 2 of the tariff book). It would be highly irregular to accept fees from the society and to charge an excess amount to the patient.

TRIAL TABLETS PROMETHAZINE/AMYLOBARBITONE (M. 241)

To the Editor: At a neuro-psychiatric clinic at Pretoria, 110 patients have been treated with trial tablets of a new preparation known as M. 241* and containing 25 mg. of promethazine and 100 mg. of amylobarbitone in each tablet.

Hitherto paraldehyde, barbiturates and chlorpromazine hydrochloride were the sedatives used at the institution in treatment or in the interim period between electro-narcosis and occupational, recreational and hypno-therapy. Because of the favourable response to M. 241 tablets, the patients have been treated either with the product alone or in combination with chlorpromazine. The following cases have been treated: Melancholia (28), alcoholism (19), psychoneurosis (15), hysteria (13, anxiety neurosis (9), depressive psychoneurosis (7), insomnia (5), confusional psychosis (3), hypochondriacal melancholia (2), back pain (2), and one case each of the following: pseudo-causalgia, addiction, psychosomatic diarrhoea, narcolepsy and cataplexy, schizophrenia, Korsakoff's syndrome, manic-depressive alcoholic.

The ages of the patients ranged from 20 to 70 years. Not more than 1 tablet was given as a single dose and the maximum daily dosage of 4 tablets was employed mainly in tension and anxiety states (in 20 patients) with significant results.

It was observed that if it was given early in the evening (the best time was found to be 8 p.m.) patients enjoyed a sound sleep and awoke refreshed the next morning. In cases of long-standing insomnia a condition resembling natural sleep was induced. Many patients volunteered the information that on awakening they did not feel any 'hang-over' effects.

Long experience with various sedatives has enabled me and my staff to assess the value of M. 241, and the results with this preparation have been so impressive that it is now employed as our routine sedative. In a small number of cases M. 241 has not been used because sedation was not satisfactory or because of personal dislike by patients. In general, patients appeared to develop less dependence on this association of promethazine and amylobarbitone than on sodium amylobarbitone alone.

In some cases of melancholia, in which dextro-amphetamine and amylobarbitone had failed to relieve the symptoms the association of chlorpromazine with M. 241 was found beneficial.

J. A. F. Denyssen

401 van Riebeek Medical Buildings
Schoeman Street
Pretoria
3 October 1957

* To be marketed under the trade name 'Protamyl'—Maybaker (S.A.) (Pty.) Ltd.